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linear PRI 12-JUL-1995
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Draft entry and computer-readable copy of sequence for [1] kindly
provided by S.H.Friend, 10:FEB 1988.
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Friend.S.B., Horowitz,J.M., Gerber,M.R., Wang,X.F., Hogenmann,E.,
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Proc. Natl. Acad. Sci. U.S.A. 84 (24), 9059 9063 (1987)
889-974.7
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/cell_type="retinoblast."
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	alatotao toaaataaaattetgeal	GCTAAAGGGGAAGTAT FACAAATGG		FGTGTCCTTGACTATTTATTAAAC	ValAlavalileProlleAsnGlys 	AlaArqIleAlaLysSluLeuGlu/ -	HischutysAsnileAsptluVall 	AsnScilkadSlyteaValThiSetAllIIIIIIIIIA 	TyrdledyrLealychad Plittillillititilliti Tacgaagaattraichtaaaat	LysThrLeuGlnThrAspSerlle? +++++++++++++++++++++++++++++++++++	AsntonAspGluGluValAsnVall 	ThrileGluGluLeuMetMetileI FFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	IleSerTyrPheAsnAsnCysThrV 	ASPILOCLYTYFILOPhotysClud HILLHHILLHHILLHLHL SAIATAGGATACATCTTAAAGAG	IledlySerdlaArqTyLDplaced HTTLLHHHHHHHHHHHHH AHGGRGGATACAACHT	LeadysSerblusluslukrqLeus TEETHIIIIIIIIIIIIIIIII CITAAAICAGAAGAAGAATTAI	DerhemismetSertentental HillHIIIIIII ATITICAIAIGECTITAIIGGE	SerThrSerGlnAsnLeuAspSerC 	CeuacsLeutysalaPbeaspPhe1

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CIGAGAAGITICCAGAAAATAAATICAGATGGTATGIAACAGGGAMMGTGTGTGAAA 2583
                                           MaTrpLeuSerAspSerProLeuPheAspLeulleLysGlnSerLysAspArgGlu 521
                                                                                                roThrAspHisLeaGluSerAlaCysProLeaAshLeuProLeuGlnAshAshHis 541
                                                                                                                                                                                                                                                                       oulysSerThrSerieuSerLeuPhc?yri.ysUasVal?yrArqLeuAlaTyrLeu 601
                                                                                                                                                                                                                                                                                                                                                                                    hrLeuPheGlnHisThrLeuGlnAsnGluTyrGluLeuMetArqAspArqHisLeu 641
                                                                                                                                                                                                                                                                                                                                                                                                                                          HnileMetMetCysSerMetTyrClylleCysLysValLysAsnileAspLeuLys 661
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161	0y 181 Met	Оу 181	Db 738 GCTAAAGGGAAGTATTACAAATGGAAGATGATGATGATTTGATTTGAGTAATGCTA 747	QV 181 C C C C C C C C C	182 ValAtaVallteProffeAshGlySerProArqfhaProArqArqsiyönAshArqSer	Db 858 ACAGCTGTTATACCCATTAA16611CACCTCGAACACCAGGGAGGGAAAAAAAGCTGTTATAA16711CACCTCGAACACCAGGGAGGGAGGAAAAAAAAAAAAAA	Oy 202 AlaAzqileafatysehnkonGhuashaspihrarqiletteettaVafik bi'ystysetiq zzi IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	QY 222 HissbackstatienspolavalLysnanvalTyrbackstatienterbehant 24 HITHTHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	Oy 242 AsnSerloadiglouValThrSerAsnGlyLcafroxluValthrBlad 261	Oy 262 TyrcludlulletyrlenbysAsnibysAspieuaspalaargieuheleuaspalisasp 281	Oy 282 LyoThilesolaThirAspSerTheoGhilhrothaArgThife AnalysSer 401 Hillillillillillillillillillillillillill	0y 302 AshlouAspoluGluvalAsnvallleProProBisTbrProValArdBrValMotAsh 321 	Oy 322 ThrileGinGinLeuwetMetileLeuAshSerAlaSerAspGinProserGinAshLeu 341 111111111111111111111111111111111	Gy 342 IloSerTyrPheAsnAsnCysThrValAsnFrcLysGUSerIleLeuhysAraVallys 461 HTTLLTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT		Oy 382 TLCCLyScrClnargfyrtystcuclyvalargicchyrtyyatgvalmetGiusormet 401 	gy 402 LeurysserdhathushuargEersserthedhatseldessertysteetheasaasaaa 421 HTHTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	Oy 422 HerberhsmetSerlicalacaRaGysAlata addavalvalmetalathrigtserara 441 Hillillillillillillillillillillillillill	QY 442 SetThrSorGluAsnLeuAspSorGlyThrAspLauSerPhoProHpHTGLUHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
2704 CTOSCAGAAAATGACTECTACTEGAACAAAAGCAAAAAGCAAAAAATGAATGATAGCATG 2763 862 AspthriserasntysGtoGtoLys 869 1111.0111111111111111111111	ATA' I AAA AA''AAAA 2787	AX 430701 48 49 bp DNA Linear PAT 09-JAN-2002	ANGROUP 1210 FOUR POTENC WOLF94629. AX 440701 GT:1810 4679	Political . Horito Sapitoris	Eukaryota: Mytazoa: Chordata: Craniata: Vertebrata: Eufeleostomi; Mammalia: Eufberia: Primates: Catarrhini; Hominidae: Homo. T	Young, P.E., Augustus, M., Carter, K.C., Ebner, R., Endress, G., Horrigan, S., Sogget, D.R. and Weaver, Z.	Caucer gone determination and therapeutic screening Using signature gene sets theory; Wo 0194629-A 1210 13 DEC 2001; Action: Person of Sets 2002	Avaion Pharmarent Pars (US) Local Configuration (Qualifiers 148 0) /organism."Homo sapiens"	74b xret-*Taxon:950b" 1534 a 502 c 880 q 1523 t	Matches:	Prof. Local Similarity: 93.4% Misma Ches: 1 Univery Match: 94.94% Indels: 59 UN: 6 Gaps: 1				GluLys GAGAAA			Aspibr 1	PhcAla [1111]

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642 ASPZIETTEMENCENCENTSECTMETTYPOLYTICCYSTYSVATLYSASMITEASPLOUTYS 661
1711 | HTTLETHTETTETTEMETTEMETTYPOLYTICCANOMACTICANOMATACACCYTANA 2297
2238 GAPPAAATTALGATGTGTTCCALGTALGGCATATCCAAACTCAACAATATACACCYTAAA 2297
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Molecular mechanisms of one ogenie mutations in timors from patients with bilateral and unilateral retinoblastoma Proc. Natl. Acad. Sci. 0.5.A. 90 (15), 7351-7355 (1993)
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       McGeo,T.L., Yandell,D.W. and Dryja,L.P.
Structure and partial genomic sequence of the human retinoblastoma
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Machanisms of oncogenesis in patients with familial retinoblastoma Br. J. Cancer 68 (5), 958-964 (1993)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Partial inactivation of the RB product in a family with incomplete penetrance of lamilial retinoblastoma and beniqu retinal tumors
                                                                                                                                                                                                                                                                                   Hemo sapiens retineblastoma susceptibility protein (RHI) mand and mutations
                                                                                                                                                                                                                                                                                                                                                                                                                                         Eukaryola; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates, Catarrhini, Hominidae; Homo.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Chadim, 2., Hogg, A., Baird, P.N. and Cowell, J.K. Obtoduric point mutations in exon 20 of the RBI gene in lamilies showing incomplete penetrance and mild expression of the retinoblastoma phenotype
                                                                  842 LeualaGlumetThrSerThrArgThrAraMetGluLysGluLysMetAsnAspSerMet 861
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               polymorphism analysis and polymerase chain reaction sequencing oncogene 7 (7), 1445-1451 (1992)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Krafizke, R.A., Officson, C.A., Hegg.A., Covon.A.B., Ceradis.J.,
Cowell,J.K. and Kaye,F.J.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Hogg,A., Onadim,Z., Haird,P.N. and Cowell,J.K. Detection of heterozygous mutations in the RB1 gene in relinoblastoma patients using single-strand conformation
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Acad. Sci. U.S.A. 89 (13), 6177-6181 (1992)
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                                                                                                                                                                                                                                                                   HKNA
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94203660
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Gene 80 (1), 119-128 (1989)
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                                                                                                                                  862 AspThrSerAsnLysGluGluLys 869
                                                                                                                                                                                                                                                                                                                                                                                                  Homo sapiens cDNA to mRNA.
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FAX: 416 813-4989

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/note-"Tumor GoSl3 unilateral frameshift mutation resulting in premature stop; Associated with this mutation is a large 13q14.3 sub-band deletion; GOO 118-734"
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                             /hote="Tumor GOS559 mutation causing premature stop.: GOO 118-734"
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/citation=[5]
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/note="G00-118-734"
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    Znote: "G00-118 744"
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                                                                                Znote-"G00-118-734"
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/replace="t"
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/replace-"t"
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VIT KFEFEYLSTIVYNYKHYHTIQYASTIPPTILSPIPHIDESPYRFDSSPLE
FROMYYTISPIKSPYKTSKOTYPPRIMTPROYTUSTGSEGTSEBRÖKTINAWCNSD
RVLKRSAEGSNIPPRYKTSKOTYPPRIMTPROYTUSTGSEGTSEBRÖKTINAWCNSD
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Ztranslation-"MPPKTPRKTAAYAAAAAPPPPPPPPPPPEDPGDSGPEDLPL
VPLEPEETEEPOFTALGOKLKIPPHPRAALTWEEVSSVDGYLGGYLGGYLGGYL
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                RLYYRVMESMLKSEEBRLSLONFSKLENDN IFHMSLLACALEVYMATYSKSTSONLOS
GTDLSFPWTLINVLNI KAFPFYKVI FSPTKAEGNI TPFMIKHLEPCEHPIMESLAMLSU
SPLEDLI KOSKDKEGPTDHLESACPLNI PLONNHTAADMY LSPVKSPKKKGSTTRVNS
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LESKLERTCELTYLTQPSSSISTEINSALVLKVSWITFLLAKGEVLQMEDILVISFQL
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SDQFSENL LSYFNNCITVNPKESI LKEVKRI GYTFKEKFAKAVGQGCVETGSQRYKLGV
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                                                                                                                                                                                                                                                                                              /product ="retinoblastoma suspectibility protein"
/protein_id="AAB59465.1"
/db vrot="01:7949995"
                                                         /orqunism="Homo_sapiens"
/db_xret="taxon:9606"
E mail: brenda thatiz.eric.on.ea.
                        Location/Onalitiers
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/note-"G00 118:7:4"
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/replace:"ea"
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Zeitation [5]
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Human rethnoblastoma susceptibility gene: cloning, identification.
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                                                                                    682 ArgValLeuIleLysGluGluGluTyrAspSerIleIleValPheTyrAsnSerValPhe 701
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Homo sapiens (clone: RB-(1,5)) foctus retina (DNA to mRMA
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Proc. Natl. Acad. Sci. U.S.A. 85 (16), 6017-6021 (1988) 88320373
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IFLDHEKTLOTISTDSFETOKIPRKSNIDEEVNITPPPPPWNITOOLMMILNSA
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VRLEFEEJ EEFPFTALCOMA (POHVNEKAM) WEAVSSVDGVIGGY (UAKKRELW) IC
TETAKVDJDEMSE ILLSYKKIYELSVHKEENLIKELOFSIKVDNAMSKLIKKYDVLFA
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RIYYEVMEŞMINSELEKIŞTONEĞKILINDILEHMILLAGALEVVMATYSKSISONIJIS
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TANAPTQATSAFQTQKPLKSTSLSLEYKKVYRLAYLALNTICERLLSEHPELEHTIWT
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EASE COUNT 1508 a 887 c 862 q 1483 t of 1483 t of 148 bp upstream of Ecokl Site; chromosome 13g14,1-q14,2.

Alequinent Scores: 5.286-308 Length: 4740
Source Smilarity: 94.11% Conservative: 2
Forcent Similarity: 94.11% Mismatches: 4
Forcent Similarity: 92.90% Mismatches: 4
Forcent Smilarity: 92.90% Mismatches: 4
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US UP U26 459A 47 (1 869) x HUMRBS (1-4740)

80	_	MetProProLysThrProArgiysThrAlaAlaThrAlaAlaAlaAlaAlaAlaGluPro 20	20
40	5.3	HI HILLING COARANG COCCOARAAA AAAAAAAAAAAAAAAAAAAAAAAAAAAA	198
ć	7.1	21 FroAlaFroProProProProProGlusluAspProtluslnAspSerGlyProGlu 40	40
3	6,6,1	199 TYGGCACGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	258
5	4.1		09
Ė	4,4,7	259 GACCEGCECTCECTCAGGETGAGGTTGAAGAAAGAAGAAGGTGATTTTAGGGATTA 318	318
Δō	£, 1	61 eysülniysizeniysileeroAspHisValArqCluArqAlaTrpleuThrTrpCluIys	80
40	£	HILLANDAAATIAAANGALACAAGATAATGICAGAGAGAGAGAGATTGATTAATTIGGGAGAAA 378	378
Ċλ	я	ValSerSerVilAspilyValfordlydlyTyrlledInLydLysGlysGluLedTrpGly 100	100
2	17.4	479 GELLOALTGEGALGGAGGAGGETALTGEAAAGAAAAAAAAGAAAGGGGGGA 438	438
7.0	101	TropstrobettoAtaAlaValAsptouAspGluMetSerPheThrPheThrGluteu 120	120
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the diagnosis of retinoblastoma 1259031-A2 1 09-MAR-1988;
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Mismatches:
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7.7	171	GlnLysAsnIleGluIleSerValHisLysPhePheAsnLeuLeuLysGluIleAspThr 140	
٩	÷.	FELLET FAVORABA FELGA FACO. 420	
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÷	107	OCTAAAGGGGAAGTATTACAAATGGAAGATGATGTGGTGATTTCATTTCAGTTAATGCTA 660	
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ž	1.6.1	TGTGTCTTGACTATITTATTAAACTGTGACCTGCGATGTTGCTCGAAGAAGAAGGATATAAA 720	
7.4	182	ValAlaValTleProfleAsuGlySe/ProArqThrProArqArqGlyGluAsuArqSer 201	
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	242	AsuserteachyteavalThrSerAsnolyteaProGluvalGlaAsnLeuSerLysArg 261 	
ē		AALTOTOTTGAACITTGTAACATGTAATGGACTTGCAAGGTTGAAAATCTTTCTAAACGA 960	
<u>></u> 4	262	: fyrchoffullefyrloutysAsrigysAspicuaspAlaargicutheicutspHisAsp 281 	
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· 4	1081	HTHTLETHTETHTETHTETHTETHTETHTETHTETHTETH	
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£	1141	ACHATCCAACAATTAATGATTTTAAATTCAGGAAGTGATGAAGCITCAGAAAATCTG 1200	_
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> ·	244	AspiledlyTyrilePhetysGluLySPheAlaLySAlaValGlyGluGlyCysValGlu 381	
<u>.</u>	197	GALALAGGALACATCITLAAAGAGAAATTTGCTAAAGCTGTGGGACAGGGTTGTGTGGAA 1320	
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5	402	Levilysserflüchüchardreiserflechnasibbeserfysteuteuasnaspasi 421	
ŝ		PETIAAATPAGAAGAAGAAGATTATGGAAATPTTAGGAAACTTGTGAATGACAAG 1440	
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qq	1441	ATTITICATATGTCTTTATTGGCGGGGCGCTCTGAGGTGGAAGAAAAAAAA	1,400
ςŏ	442	SerThr SerGlnAsnleuAspSerGlyThr AspleuSer Phetrolroll (cleuAsnVal)	4 6.]
QQ	1501	AGIACATCICAGAAICTIGAITCTGGAACAGATTGGTCTTTCCCATGGATTTGTTTT	15,6,0
οχ	462	LeuAsniceulysAlaPheAspPheTyrLysVallledluserPhellelysAladludly	4 H I
035	1561	CTTAATTTAAAAGCTITGATTTTACAAAGTGATCTTTTTTTTTT	1625
Ś	482	AsnLeuThrArqGluMetHeLysHisLeuGluArafysgluHisArafleMetGluSer	501
Q	1621	AACTTGAGAAGAAATGATAAAAGATTTAGAAGGATGTGAACATGGAATCATGGAATCC	1680
ολ	502	JeuAla p.	523
Q	1681	CTEGCATGGCTCTCACATTCACCTTTATTTGATCTTA1TAAACAATCAAAAGAAAA	1740
 62	(1) (1) (2)	ClyproThrAsplisLenGlaSerAlaCysFraLenAsuLentrale ashaAsmAsmlis	14.
10 b	1741	GGACCAACTGATCACCTTGAATCTGCTTGTCTTAATCTTCTCTCTC	1800
ςò	542	ThralaalaaspwetTyrLeaserProValAraserProJystystystystystyfftr	195
qq	1801	ACTGCAGCAGATATGTATCTTTCTCCTGTAAGATCTCCCAAAGAAAAAAGGTTCAACTAGG	1860
οy	562	Arqva I Asnsec Thr Ala Asna I agu a tha Ghalla Three Ala Pheol in three mhys '	H
d G	1861	GGTGTAAATTCTACTGCAAATGCAGAGACACAAGCAACCTCAGCTTGCAGACCCAGAAG	1920
ογ	582	ProLeuLysSerThrSerLeuSerLeuPheTyrLysLysValTyrArd.euAlaTyrLeu	601
qq	1921	CCATTGAAA1CTACCTCTTTCACTGTTTTATAAAAAGTGTATTGTTTTTTTT	1980
ογ	602	ArgLeuAsnThrLeuCysGluArgLeuLeuSerGluHisProGluLeuGluHisIleIle	621
QQ	1981	COSCIDADATACACITICICAACOCCITCICICAGACACACACATACATC	2040
ολ	622	TrpTbricuPheCluHistbricachAsachatyrGluLeuMetArqAspArqHiston	6.4.1
qq	2041	TGGACCCTTTCCAGCACCCTGCAGAATGAGTATGAACTCATGAGAGAGA	2100
ð	642	AspGlalleMetMetCysserMorTyrilyTheTystysVallysAssHoAspLortys	661
11 b	2101	GACCAAATTATGATGTGTTCCATGTATGCCAAAGTGAAATATATAT	2160
ς	662	PheLysllelleValThrAlaTyrLysAspteuProHisAlaValGhuGhThrPheLys	681
 q	,2161	TICAAAATCAITGIAACAGGATACAAGGATCITCCTCATGCTGTTCAGGACATTCAAA	2220
Ολ	682	ArgVall.cu1fet.ysGluGluGluTyrAspSer11e11eValPhetyrAsnSerValPhe	701
â	2221	CGTGTTTTGATCAAAGAAGAGGGTATGATTGTATTATAGTATTCTATAAATAA	2280
Ś	702	MetGlnArqLeuLysThrAsnIleLeuGhlyrAlaSerThrAraBroProThilanser	7.21
q	2281	AFGCAGAGACTGAAAAAAAATATTTTGCAGTATGCTTCCACCAGGCCCCTTACTTGTCA	2 440
ć	C1	ProlleProllis1leProArqSerProTyrLysPheProSerSerProLeuArq1lePro	741
qa	2341	CCAATACCTCACATTCCTCGAAGCCTTACAAGTTTCCTAGTTCACCTTACGAATTCCT	2400
9,	742	OlyClyAssileTyrileSerProtestysSerProfythysHeSerGladiyLenPro	76.1
QD	2401	GGAGGAACATCTATATTTCACCCTGAAGAGTCCALATAAAALTTCAGAAGGTCTGCCA	2460
:5 £	762	762 ThrProThrLysMetThrProArgSerArgIdeLeavalGerileatyGlader Phedly 781 [11] [1] [1] [1] [1] [1] [1] [1] [1] [781
G.	- : - :	ACACCAACAAAAA LOACI CCAAGA LCAAGAA ICI I ACIA I CAA I HOLIAA ICAA I LOAGA	07.7
ć	782	ThrSerGluLysPheGlaLysTleAsnGlaMetValCysAsnSerAspA.qValLoaLys	801

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                                                    252] ANTICIGAGAMSTIPPMAAAAIAAAAIAAAPPMASSSATAISSAABSSAASSIGIGGEGAAA 2580
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                                   802 ArqSetAlaCluClySetAsnProProLysProLeuLysLysLeuArgPhcAspileGlu 821
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Eryja,T.P., Friend,S. and Yandell,D.
DIAGNUSES OF RETINGLASTOMA
Patent: WO 8906704-A | 27 TH. 1989,
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141 SerThriysValAspAsnAlaMetSerArgLeuLeuLysLysTyrAspValLeuPheAla 160
                                                      161 LeuPheSerLysLeuGluArgThrCysGluLeuIleTyrLeuThrGlnProSerSerSer 180
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A01444 PARTON 4.6 Kb retinoblastoma gene probes. A01444
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A method for detecting the predisposition to retinoblastoma and a
method for detecting a retinoblastoma gene in tumors using a
                                                                                                                                                                                                                                                                                                                                                             Eukaryola, Metazoa, Chordata, Craniata, Verfebrata, Eutheleostomi,
Mammalia, Eutheria, Primates, Catarrhini, Hominidae, Homo.
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                                                    258] AGANGTGCTGAAGGAAGCAACCCTCCTAAACCACTGAAAAAACTACGTTTCATATTGAA 2440
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Patent: EP 0293266.A 1 30.NoV-1988;
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λ. 4.	227	AspüluValLysAsnValTyrPheLysAsnPhelleProPheMetAsnScrLeuGlyLeu 24 	.6)1
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5~ ⊕	467	PhotysciutysPhoAlalysAlaValOlyCinClyCysValCluttctySerGinArg 38 	20
<u> </u>	1421	TyrtysLewslyValAraLewTyrTyrAxaValMetsLuserMetsLewLysSetsluGlu 40 	
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qq	1381	GAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTTATATGTCT	1440
Oy	427		446
qq	1441	TTATTGGGGGGGGTGTTTTTATTATTGTTTTTTTTTTT	1500
ò	447	LeudspSerGlyThrAspLeuSerPheProTrpIleLeudsnValLeudsnLeudsnleudysdla	466
qq	1501	CITIGATITCAGGAACAGATITFGIGTITTCCCATGGATICTGAATGTGCFTAATTTAAAAAGCC	1560
07	467	PheAspPheTyrLysVal TleGluSerPheHetJetysAlaGluGlyAsnLeuThrArgGlu	486
qa	1561	TTTGATTTTTACAAAGTGATCGAAAGTTTTATGAAAGCAGAAGGGAACTTGACAAGAA	1620
ОУ	487	MctllclysHistouGluArgCysGluHisArglleMetGluSerLeusAattpLeuSer 	300
qu	1621	ATGATAAAACATTTAGAACGATGTGAACATGGAATCGAATGGAATGCTTTTGCATGGGTCTCA	1680
òy	203	AspSerProLeuPheAspLeuIleLysGlnSerLysAspAraGluGlyProThrAspHis	475
ĝ	1681	GALTCACCTTTATTTGATCTTATTAAACAATCAAAGGACGGAGAAGGACCAACTGATGAC	1740
οΣ	527	LeuCluSerAlaCysProLeuAsnLeuProLeuClnAsnAsnHisThtAlaA:aAspMet	546
qq	1741	CTTGAATCLGCLLGTCCTTAATCTTCCTCCAGAALAATCACAGAGAGAATATG	1800
ŎŇ	547	TyrleuSerProValArgSerProLysLysLysClySerThrThrArgValAsnSerThr	566
qu	1801	TATCTTTTCTCTGTAAGATCTCCAAAGAAAAGGTTCAACTACGCGTGTAATTCTACT	1860
Qy	267	AlaAsnAlaGluThrGlnAlaThrSerAlaPheGlnThrGlnLysProLeuLysSerThr	586
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ΟŊ	607	CysGluArgleuleuSerGluHisProGluieuGluHisllelleTrpThrieuPheGli	974
q _O	1981	TOTICAACGCCTTCTGTGTGTGTCCAGAATTACAACATATCATCTGCTGTGTGTG	2040
Qy	627	HisThrLeuGlaAsnGluTyrGluLeuMetArqAspArqHisLeuAspGlu1leMetMet.	646
qu	2041	CACACCTGCAGAATGAGTATGAAGTCATGAGAGAGAGGGATTTGGAGGAATTATGATG	2100
Οy	617	CysserMetTyrClylleCyslysVallysAsmileAsplantysPhelysHelleVal	999
qq	2101	TGTTCCATGTATGGGATATGCAAGTGAAGTATAGACTTAAATTCAAAATGATGTA	2160
QY	667	ThralaTyrlysAspicuProHisAlaValGlnGluThrPheLysArgValLeufleLys	686
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Db	2340	GCTCGAAGCCTTTAGAAGTTTCCTACTTCACCCTTTACCGATTCCTGGACCAACALGLAL	2349
ò	747	IleSerProLeuLysSerProTyrLysIleSerGluGlyLeuProThrProThrLysMet	766
qu	2400	ATTTCACCCTCAACACCCATATAAAATTTCAGAAGTCTGCCAACACACAAAATG	2459
OY	167	ThribroArgSetArg11eLeuVa1Set11e31y31u3e1Phe31y1ht3e+51uiysPhe	386
qq	2460	ACTCCAAGATCAAGAATCTTAGTATCAATTGGTGAATCATTCGGGACTTC1 GAGAAGTTC	2519

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981 AATTGACTFGGAATTGTATCATGTAARGGATGGAAAGGTTGAAAGGC 1040
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               201 GAGCIGCERCTGGGRAAGATITGAGTTTGAAGAAATIGAAGAAGERGAATITATTGATTA 260
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1 MetFroProLysThrFroAraLysThrAlaAlaThrAlaAlaAlaAlaAlaAlaaluPro 20
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	541	OlyProthraspHisterGlusorAldYsProtestanterProtectation		5 3
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	481 1700	LeuAsnLeuLysAlaDheAopPheTyrLysValIleGluScrPheIleLysAlaGluGly -	end	5 🕏
	461 1640	SerThrSerGinAsnLeuAspSerGlyThrAspLeuSerPheProTrpIleLeuAsnVal 	7.	3 8
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	321 1220	2 ASHLOHASPGTUGTUVATASHVATTTEPTOPTOVATARGTPTVATARGTPTVATMETASH 		5 1

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682 ArgValLeuIleLysGluGluGluTyrAspSerIlcIlcValPheTyrAsnSerValPhe 701
                                                                                                                     762 ThrProThrLysMetThrProArgSerArglleLcuValScrilLGlyGluSerPheGly 781
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742 01/01/7AssileTyrileSerFroLouLysSerFroTyrLysileSerGluGlyLeuPro
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662 PhetystletleValThrAlaTyrtysAspteuProHisAlaValGInGluThrPhetys 681

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GenCore version 5.1.3
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January 16, 2003, 15:20:17; Scarch time 499.872 Seconds (without alignments) 17531.794 Million cell updates/sec 1 GCCGCATGTCAAGACTGTL.....AAAJGAGGATTATTGATAGT 3113 foral number of hits satistying chosen parameters: 2185239 seqs, 1125999159 residues modele search, using sw model IDENTITY NUC Gapop 10.0 , Gapext 1.0 US 09 026 459A 86 3113 Maximum 194 seq length. Zoonooninin Post processing: Minimum Match U% Minimum DB seeq length: 0 Perfort Score; Scoring table: one letter Sentimenters Seatched: Pull off:

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result being printed, is the number of results predicted by chance to have a score greater than or equal to the score of the result bein and is derived by analysis of the total score distribution. Fred R

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Benedict WF, Hu S, Xu H, Zhou Y;

Modified retinobla DNA sequence of the	human retinoplasio Human androqen rec Breast cancer rela	Human retinoblasto	Human retinoblasto	Human retinoblasto	Retinoblastoma 94k	Probe for relinobl	Modified retinobla	cONA of human reti	Modified retinobla	Modified relinobla	Modified retinobla	Cancer Supressing	ketinoblastoma qen	Retinoblastoma pro	Wild type human re	Human pilo RB reti	CDNA encoding a re-	Retinoblastoma tum	Retinoblastoma tum	Retinoblastoma tum	Retinoblastoma tum	Human Rb110 cDNA.	Human retinoblasto	DNA of human retin	Antisense sequence	birect tandem repe	Perstner pMK10,7AS	Construct pMK10,7AS	Canstruct pMK10/AS	Retinoblastoma pro	Motinoblastoma pro
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Modified retiroblastoms tampor suppressor, FTSF protein, cancer therapy; cellular proliferation inhibitor; ss. Modified retinoblastoma tumour suppressor gene. Location/Qualifiers 7..2352 AAV58445 standard; DNA; 3113 BP. (BAYU) BAYLOR COLLEGE MEDICINE (TEXA) UNIV TEXAS SYSTEM. 98WO-US03041. 97US-0038118. minute 1998 (tirst cetry) /*t.ag- a Homo sapiens W09837091-A2 19-FEB-1998; 20-FEB-1997; 27 - AUG - 1998 AAV58445; RESULT 1 Key AAV58445

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                                                                                                                                                                                   provein (RISP) of the invention. The proteins can be used for inhibiting profess profiteration, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular profiteration, particularly cancers. The RISPs have a broader spectum of
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                                                                                                                                                               this sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                          100.0%; Score 3113; DB 19; Length 3113; 100.0%; Pred. No. 0.
                                                         Refinoblastoma suppressor protein with N-terminal modification ishibiting ceilular proliferation, particularly cancer
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                                                                                                                       laim 22: Page 173 177; 249pp; English.
                                                                                                                                                                                                                                                                  activity than wild type RTSPs.
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1998-480788741.
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                                                        2941 CIGIGIGCTIVITITIAIAAATITIGCITTIAATIAAATAAAAGCIGGAAGCAAGIAIA 4000
                                     The present sequence appears in the specification, which describes a retracycline responsive expression vector (TREV), which contains a sequence encoding a fusion protein comprising a transcriptional transactivation domain (TIP) operatively attached to a tetracycline repressor protein (TRP), the first sequence operatively positioned downstream of a promoter. The vector also contains a cloning site operatively positioned downstream of a basal promoter comprising a tetracycline operator. The TREVS can be used to produce stable cell
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Gaps
                                                                                                                                                                                                                                                                                                                                                                                Minimal promoter, tetracycline responsive expression vector; TREV;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  tightly controlled expression of genes, such as tumour suppressor genes for treating cancers
                                                                                                           3061 ACTGATTATTTTCTTCATCCAACTTATGTTTTAAATGAGGATTATTGATAGT 3113
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      99.8%; Score 3107; DB 19; Length 3218; 100.0%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 New tetracycline responsive expression vectors - used for the
                                                                                                                                                                                                                                                                                                                                                                                                               Letracycline repressor protein; TRP; tetracycline operator; production; stable cell line; protein production; tamber suppressor protein; treatment; cancer; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      by abnormal cellular proliteration, particularly cancers.
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                                                                                                                                                                                                                                                                                                                                                                                                transcriptional transactivation domain; TTD;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Query Match 99.8%; Score 3107; DB Best Local Similarity 100.0%; Pred. No. 0; Matches 3107; Conservative 0; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Disclosure; Pages 153-157; 190pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Zhou Y;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Location/Qualifiers
7..2457
/*tag- a
                                                                                                                                                                                                                                                                                                                                            DNA sequence of the specification.
                                                                                                                                                                                                                                 AAV54991 standard; DNA; 3218 BP
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2587 AGLIGLAD/AGAITGTTICTLCCAAAGTAAAATTGCTGTGTTTATGGAYAGTAAGA 2646
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2272 CTFPTAAACGATGAAAAAACTACGCTTTGATATTGAAGGATCAGATGAAGCAGATGGA 2331
                                                     2.492 GGAACACGAA EGCAAAAAGCAGAAATGATGATAGCATGGATACTCAAACAAGGAAGAG 2451
                                                                                                                                                                                      2.477 AAATGAGGALTIPAGGAPET IGGTGGACACTGTGTACACPTFFGATTGATTGTCTCTCTCA 2406
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                                                                                                             2247 CHANDANANATONAAANONAAAATGAATATANONTGGATAOGOTGAAAQAAGGAAGA
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                                 2227 ACHAAACATCHOCHAGGAGAGTCCAAATTTGAGGAGAAAGTGGGAGAAATGACTTCTACT
                                                                                                                                                                                                                                                                                    8067 TAFFFFFFFFFFALGAAGTTATAAATGAGGATFAFFGAFAYF 3113
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Modified retinoblastoma tumour suppressor; KISP profein; cancer therapy;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Sequence 3266 BP; 1092 A; 602 C; 574 G; 998 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                           inhibiting cellular proliferation, particularly cancer
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                                                                                                                                                                                                                                                                                                                                                                                                                                                          Claim 22; Page 166-170; 249pp; English.
                 cellular proliferation inhibitor; ss.
                                                                                Location/Qualifiers
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Modified retinoblastoma fumour suppressor: RTSP protein, cancer therapy;
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This sequence encodes a modified retitublishem tumour suppressor protein (RTSP) of the invention. The protein can be used for inhibiting cellular proliferation, when coadministered with a ptv protein. The RTSPs can be used for treating diseases characterised by abnormal cellular.
                                                                              proliferation, particularly cancers. The RTSPs have a broader spectrum of
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                                                                       367 GAAAATGATACAAGAALLATTGAAGTTCTCTGTAAAAAACATGAALGTAATALAAATGAATATAAA 426
                                                                                                                                              427 GIGAAAAAIGITIAHTICAAAAAHTITATAPOHTITIALGAATTOTOHOGAYHTGIAACA 486
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                                                                                                                                                                                                                                                                                             547 AATAAAGATCTAGATGCAAGATTATTTTGGATGATGATAAAAGTGTTAGAGACTGT 606
                                                                                                                                                                                                                                                                                                                                                                                  757 AATAAAGATCTAGATGCAAGATTATTTTGGATGATGATAAAACTCTTCAGACTGATTCT 818
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15.37 TOTGOTTG FORTOTTANTOTTCOTOTCAGAATAAIFCACACAGCAGCAGATATGTATGTT 1596
                                       1 887 TOTCOTGTAAGATOTOCAAAGAAAAAGGTTCAACTAAAGGTGTAAATTCTAGTGCAAAT 1446
                                                           15-37 TCTCCTGTAAGATCTCCAAAGAAAAASTTFCAACTACAACTACAAATTCTACTACAAT 1656
                                                                                                                 1657 GCAGAGACACAACCATCATAGCTTCTAGACCAAGCTTGAAAATGTAGTTTGAAAATGTACTCTCTT 1716
                                                                                                                                                                                                 1987 ICACTGITITATAAAAAGIGITATGGGCTAGCCTATCTCCGGCTAAATACACTTTGTGAA 1566
                                                                                                                                                                                                                                    1/17 ICACIGITITATAAAAAAGTGTATGGGGTATGTGCGGGCTAAATACACTTTGTGAA 1776
                                                                                                                                                                                                                                                                           1957 ONCOTTOTATATAGGACACAGAATTAGAACATATGATGTGGGAGGGTITIGGGAGAGAGG 1626
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Modified retinoblastoms tompor suppressor, RTSP profeio, cancer therapy, cellular proliferation inhibitor; ss.
               2677 CTTTTGTGGATATAAAATGTGCAGATGTGTGTGGGGGGATGATGCTAAGCGAGTGAA 2736
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                                                                                                 2737 ATCTTACTCAPTCTTTATTTTACAAGATTGGAAATCTTCTAAATCTCTAAATCTCTAAATTTAAAA 2796
                                                                                                                                    2587 AGTIGIAGGAGAIIGIIIGGIGIFGGAAAGTAAAAIIGGIGGGIIIAIGGAIAGTAAGA 2646
                                                                                                                                                                                                    2647 ATGGGCGTAGAGTGGGAGTCCTGATAACGGAGTGTGTGAGTAGTTVGGGTTGTTTG 2706
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                                                                                                                                                                                                                                                                                                                                                                    3217 IGATACTATCATACTACTGAAACAGATTTCATACCTCAGAATGTAAAAGAACTTACTGAF 3276
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                                                                                                                                                    2467 PITITIRGIOGATALAAAATGIGGAGTGCAATIGTITICCGIGATICCIAACQCAATIGAA
                                                                   2527 ATCTTACTCATTGTTATTTATACAAGATTGAAAATGTIGTGAAATGCTGGGGATTFAAAA
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                                                                                    3067 TAPPPPPCTTCATCCAACTTATGTTTTTAAATGAGGATTATTGATAGT 3113
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Retinoblastoma suppressor protein with N terminal modification
                    Zhou Y;
(HAYU ) BAYLOR COLLEGE MEDICINE
                   Benedict WE, Hu S, Xu H,
      (TEXA ) UNIV TEXAS SYSTEM.
                                1998 480788/41
                                        P. PSDB; AAW69366
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inhibiting cellular proliteration, particularly cancer

"Laim 22: Page 150 155; 249pp; English.

protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p54 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular. proliferation, particularly cancers. The KTSPs have a broader spectrum of This sequence encodes a modified retinoblastoma tumour suppressor activity than wild type RISPS.

Sequence 3392 BP: 1137 A: 514 C: 507 G: 1034 T: 0 other;

0 585 127 GCATTGGTGCTAAAAGTTTCTTGGGACATTTTTATTAGCTAAAAGGGGAAAGTATTACAA 186 406 GCATTGGTGGTAAAAGTTCGTTGGALCACATTTTTATTAGCTAAAGGGAAGTTATTACAA 465 AFGGAAGATGATCTGGTGAFTTCATTTCAGTTAATGCTATGTGTCCTTGACTATTTATT 525 247 AAACHOLOAGGTGGGATGTLGGTGAAAGAACCATATAAAACAGGTGTTATAGGGGATTAAT 306 967 GAAAATGATAATAATTAATTGAAGTTCTCTGTAAAGAACATGAATGTAATATAGATGAG 426 4.27 @GGAAAAAUDTTATTCAAAAATTTATACPETTTATGAATTCTCTGGACTGGAAAA 486 205 GEGAAAAATGITIAITTCAAAAATITIAATAGGITTTATGAATTCTGGGCTTGTAAGA 765 487 ICTAATGGACTTCCAGAGGTTGAAAATCTTTCTAAAAGAATACGAAGAAATTTATCTTAAA 546 47 AATAAAGATCTAGATGCAAGATTATTTTGGATCATGATAAAACTCTTCAGACTGATTCT 606 426 AATAAAGATCTAGATGCAAGATTATTTTTGGATCATGATAAAACTCTTCAGACTGATTCT 885 507 ATAGACACTELLEGAAACACAGAACACGAAAAAAGEAACCTTGATGAAGAGTGAAT 666 667 GTAATTCCTCCACACACTCCAGTTAGGACTGTTATGAACAACTATGAACAATTAATGATG 726 286 ATGTCAAGACTGTTGAAGAAGTATGATGTTTGTTTGCACTCTTCAGCAAATTGGAAAGG 345 546 GAAAATGAFACAAGAATTATTGAAGTTCTCTGTAAAGAACATGAATGTAATATAGATGAG 0; Gaps 7 ATGTCAAGACTGTTGAAGAAGTATGATGTATTGTTTGCACTGTTCAGCAAATTGGAAAGG 66 39.8%; Score 4107; DB 19; Length 3392; Indels :, O 0; Mismatches Pred. No. 0; Local Similarity 100,08; Conservative Matches 3107; Lonerty Materia â څ 5 Ē 5 5 ŝ ŝ = 5 Ê 5 $\frac{\tilde{\Xi}}{\tilde{\Xi}}$ ŝ = 5 ÷ 5 5 ŝ $\tilde{\Xi}$

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1608 TOTOCHTGREGOTGTTVANTOTTTGCTGTGCGGGAATAATGCACACTGCACCACATAIGIAITT 1665
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                     126 GAGAAATTGGTAAAGGIGTGGGACAGGGTGIGICGAAATIGGATGACAGGATAAA 1185
                                                                           787 ACAGTGAATCCAAAAGAAGTATACTGAAAAGGGTGAAGGGATATAGGATACTFTAAA 846
                                                                                                                                                         847 GAGAAATTTGCTAAAGCTGTGGGACAGGGTTGTCTCTCGAAATTGGATGCATACAAA 906
727 ALELEAALICAGCAAGIGAICAACETICAGAAALCEGATETCOEATITEAACAACTGC 786
                                                                                                                                                                                                                                                                           1207 AAACATTTAGAACGATGTGAACATCGAATGAATGCCTTGCATGGCTCTCTCAGATTCA
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This sequence enoughs a rediffed retingularional turner represent protein (MTSP) of the invention. The proteins can be used for inhibiting cellular problication, when coadministered with a p53 protein. The KISPs can be used for treating diseases characterised by abnormal cellular profiferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Modified retimoblastoms tumbur suppressur: RISF protein, cancer therapy: cellular prollieration inhibitor; ss.
3166 AAAAATTACTAATTTTACACATTAGATTTTATTACTATTGGAATCTGATATACTGTGT 3225
                                                                                                                                                                                                                                               3286 IGATACIAICAIACIACIGAAACAGAIIICAIACCICAGAAIGIAAAAGAACIIACIGAI 3345
                                                                               2947 GCTTGTTTTATAAAATTTTGCTTTTAATTAAATAAAAGCTGGAAGCAAAGTATAACCATA 3006
                                                                                                                                     3007 TGAMACTATCATACTACTAAAACAGATTTCAMACAARGAARGTAAAAGAACTTACTGA
                                                                                                                                                                                                                  Retinoblastoma suppressor protein with N-terminal modification
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           inhibiting cellular proliferation, particularly cancer
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Modified retinoblastoma tumour suppressor: RTSP profein; cancer therapy;
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                                                                                                                                                2865 STEELGEGGGATATAAAATGEGGGGATTGGGGTGATTGCTAAGGCGACTTGAA 2868
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Tellular proliferation inhibitor; ss.
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This sequence encodes a modified retincblustoms tumbour suppressor protein (RISP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coordministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 TOTAATGGAOTTCCAGAGGTTGAAAATOTTTCTAAAGGATACGAAGAAATTTATCTTAAA 546
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               475 GCATTGGTGCTAAAAGTITCTTGGAICACAITTTTATTAGCTAAAGGGGAAGTATTACAA 534
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                                                                                                                                                                                                                                                                                                                                                                 Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           DB 19; Length 3461;
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                                                                                                                                                                                                                                                                                                                                                                                                                     Claim 22; Page 188-192; 249pp; English.
Location/Qualitiers
                                                                                                                                                                                                                                                                           Hu S, Xu H, Zhou Y:
                                                                                                                                                                                                                     (BAYU ) BAYLOR COLLEGE MEDICINE.
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                                                                                                                                                                                                                                                                             Benedict WF,
                                                                                                                                                19-FEB-1998;
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Oy Dp	1627	CTGCAGAATGAGTATGAACTCATGAGAGACAATTTGAGACCAAATATGATGGTTGC 	1686 2044
ΟY	1687	ATGLAT GGCATATGCAAAGTGAAGATATAGACCTTAAA TTCAAAALCATTGTAACAGA	1746
qa	2035	A I GTATGGGATATGGAAAGTGAAGATATAGAGCTTAAATTGAAAATGATTGTAAGAGA	2044
y g	1747	TACAAGGATCTTCCTCATGCTGTTCAGGGGGACATTCAAAGGGGTTTTGATCAAAGAAGAGG FULLILIHTHTTTTTCTCAGGGGGGGGGGGGGGGGGGGGGGGGGGGG	1806
ογ	1807	GAGTATGATTCTATT AVAGTATTCTAVAACTGGGTCTTCATGCAGAGACTAAAAATAAAT	1866
q 0	2155		2214
Oy	1867	ATTITIGGASTATISCI INCACCAGGCCCCCTACCI IGITACCAALACTAATATTTTTERS	9761
qu.	2215	ATTITICAGIATIGET CONCONCIONAL ACCIDATA ACCANA ACCIDATA TOTAL CALLES	2274
.ó .: 	1927	AGCCTTACAAGTTCCTAGTTCACCCTTACAGATTCCTGGAGGAACACTATATTCA	1986
a a	2275	AGCCTTACAAGTI ICCTAGTTCACCTTTACGGALICTIGGGGGAAAATTTALALITGA .	23.44
o d	2335	CCCCTGAAGAGTCCATATAAAATTTCAGAAAGTTTTGCTAACAAAAATGACTGA TTTTTTTTTATTTTTTTTTT	2046
ογ	2047	AGATCAAGAATCTTAGTATCAATTGGTGAATCATTGGGGACTTCTGAGAADTTCCAGAAA.	2106
10 b	2395	HITTELLETTELlettel	44.47
ò	2107	ATAAATCASATGSTATGTAACASCGACCSTGTGTGTCAAAASAAGTSCTCAAGSAAGTAACTA	2166
qu	2455	ATAMATCAGATIGETATGTAACAGCGACGETGTGCTCAAAAGAAGTGCTGAAGGAAGTAACT	2514
QY	2167	CCTCCTAAACACTCAAAAAACTACGCTTTGATATTGAAAGATGAAALGAAGAGAAGA	2226
qq	2515	CCTCCTAAACACTGAAAAAACTACGTTTGATATTGAAGGALCAGAGGAAGAAGATGGA	2574
OY	2000	AGTAAACATCTCCCAGGAGAGTSCAAATTTSAGAAATTGGAAAAAAAAAA	2286
q 0	2575	AG FAAACATCTCCCAGGAGAGTCCAAATTT CAGGAGAAATTGAGTTTTTTTTTT	26 44
ć	2287	CGAACACGAATGCAAAASCAGAAATGATGATGASATGSAATACGTCAAA AASAAGAG :	2146
qq	2635	CGAACAGAATGCAAAAGCAGAAATGAATGATAGCATGGATAGCTCAAAGAAGAAGAGT	2694
οy	2347	AAATGAGGALCTCAGGACCTTGCTGCACACTGTGTACACCTCTGGALLCALLGTCTCTCA	2406
qq	2695	AAATGAGGATCTCAGGACCTTGGTGGACACTGTGTACACTGTGGATTCATTGTCTCTCA	2754
OY	2407	CAGATGTGACTGTATAACTTTGCCAGGTTGTGTTTATGGCCACATTTAATATCTTAACTT	2466
qq	2755	CAGATGIGATGIATAATTITOOPAGITGIGITATGGGGGAATTIAATATGTTOOPAGTTI	2H 14
ò	2467	CTTTTTGTGGATATAAAAIGTGCAGATGCAATTGTTTGGGTGATTCCTAAGCCACTGGA	15.26
qu	2815	CITTTTGFGGATAFAAAATGFGCAGATGCATTGTTTGGCGATTGTTTTTTTTTT	2874
ολ	2527	AFGERAGICALTGITATT IATACAAGA ITGAAAATEETGI GI AAATEET GAAA.	2586
đđ	2875	AIGITAGTCATTGTTALLIALACAAGALGAAAALGTGGGAAALGCGGGGAATTTAAAA	29.44
QY	2587	ACTIGIACCACATICITICCICITICCAAACTAAAATICCTOTOTOTOTATAAAAAAAAAA	2646
qo	2935	AGTTGTAGCAGATTGTTTGCTCTTGCAAAQTAAAATTGCTGTGTGTTTATGTATAGTAAGA	7667
ς	2647	ATGGCCCTAGAGTGGGGGTCCTGATAACCCAGGCTGTCTGT	2706
qu	2995	ATGCCCTAGAGTCGGGAGTCCTGATAACCCAGGCTGTTTTTTTT	1054

proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.

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This sequence encodes a modified relinoblastoma tuniour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when condministered with a p52 protein. The Pugps can be used for treating diseases characterised by abnormal cellular.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Modified retinoblasiona tumour suppressor, RTSP protein, caucer therapy, cellular proliferation inhibitor; ss.
2947 GCTTGTTTTATAAAAITTTGCTTTTAAITAAATAAAAGCTGGAAGCAAAGTATAAGGTA 3006%
                                                            2767 AACATGAACACCTTAGAAAATGTCTCTATCTATCTTTCTATCCAAATGGACTG 2826
                                                                            2887 AAAAATTACTAATTIFACACATTAGATTTTTATTTACTATTGGAATCTGATATACTGTG 2946
                                                                                                                                                                                                       3.25 GC11G1111AFAAAAT111GC1111AA1TAAATAAAAGCTGGAAGCAAAGTATAACCATA 3354
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                               2827 CCCATTCACCAAAATTAFCCTGAACTCTTCTGCAAAATGGATATTATTATAGAATTAGAA 2886
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                      3067 TATTITICTICATCCAACTTATGTTTTTAAATGAGGATTATTGATAGT 3113
                                                                                                                                                                                                                                                                                                                                                                                           mhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Modified retinoblastoma tumour suppressor gene.
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5 G	16.27 2068	CTOPAGAATGAGTATGAACTCATGAGAGACAGGCATTTGGAGGGAATTATGT 	16 21
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5 G	1747	TACANGATETTCEFATGETGTTEAGGAGACATTCAAACGTGTTTGA 	18
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                                                                                                                                                                                                                                                 Medilied retinoblastoma tumour suppressor; RTSP protein, cancer therapy;
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487 TCTAATGGAGTTTCCAGAGGTTGAAAATCTTTCTAAACGATACGAAGAATTTATATGTTAAA 546
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2527 ATGTTAGTGATTGTTATTTATAGAAGALIGAAAAICHIGTGTAAAHTTGTGTGAFTTAAAA 2586
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Minimal promoter; tetracycline responsive expression vector; TREV; transcriptional transactivation domain; TTD: tetracycline repressor protein; TRP; tetracycline operator; production; stable cell line; protein production;
               1088 AFGGCCTAGAGTGGGAGTCCTGATAACCCAGACTGTCTGACTACTTFGCTTCTTTTG
                                                                                                                                                                           2707 TAGGATATAGGTGALG1FTGCTGTTTTTTTTTAAT1TATAALG1A1AT1TTLTAAT11
                                                                                                                                                                                                                                      3388 GCTTGTTTTATAAAATTTTGCTTTTAATTAAATAAAGCTGGAAGCAAAGTATAACCA
                                                        2587 AGTEGFAGGAGATEGELECCECETEGGAAGFAAAATEGGEG OOT FEAGGATAGAAGA
                                                                                                                 2647 ATGGCCCTAGAGTGGAGAGTCCTGATAACCCAGCCCTCTCTCACTTTTCCCTTCTTTTC
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                                                                                                                                 3067 TATTTTCTTCATCCAACTTATGTTTTAAATGAGGATTATTGATAGT 3113
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  tumour suppressor protein; treatment; cancer; ss
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operatively positioned downstream of a basal promoter comprising a letracycline operator. The TREVs can be used to produce stable cell lines in which gene expression is tightly regulated by tetracycline. They can be used for the production of proteins such as tumour suppressor proteins which can be used for the area for treating discusse characterised.
                                                                                                                                                                                                                                                                        The present sequence appears in the specification, which destities a retracycline responsive expression vector (TREV), which contains a sequence encoding a fusion protein comprising a transcriptional transcriptional (TDA) expression acts and the contains transcription demain (TDA) exertainely attacked to a tetracycline repression protein (TRE), the first sequence appears to promoter. The vector also contains a cloning site
                                                                                                                                      New fetracycline responsive expression sectors used for the tightly controlled expression of genes, such as tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                by abmormal cellular proliferation, particularly cancers.
                                                                                                                                                                                                                                dischasure: Pages 145 150, 190pp, English.
                      Xu H, Zhou Y;
                                                                                                                                                                                      genes for treating cancers
                      Loquithet is CJ,
                                                                WPI: 1998 480796/41.
                                                                                         P PSDB; AAW71354.
                      H. S.
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Sequence 3555 BP; 1171 A; 684 C; 653 G; 1047 T; 0 other;

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988 AATAAAAGATCHAGAAGATTTTTTTTTTTGGATGATGATAAAACTCTTCAGAGTGATTCT 1047 928 ICTAAIGGACTICCAGAGGTIGAAAATCTITCIAAACGAIACGAAGAAAIITAICIIAAA 987 187 ATGGAAGATGATGTGGTGATTTGAGTTAATGGTATGTGTGTGTGTGATTTTATT 246 428 AIGGAAGAIGAICIGGGGGATTICATTICAGTIAAGGTATGTGTGTCCTTGACTATTITATT 687 46.7 GAAAATGATACAAGAATTATTGAAGTTCTCTGTAAAGAACATGAATGTAATATAGATGAG 426 427 GTGAAAAATGTTTATTTCAAAAATTTTATACCTTTTATGAATTCTCTTGGACTTGTAACA 486 487 ICTAATGGACTTCCAGAGGTTGAAAATCTTTCTAAACGATACGAAAATTTATGTTAAA 546 547 AATAAAGATCTAGATGCAAGATTATTTTTGGATCATGATAAAACTCTTCAGACTGATTCT 606 ATAGACAGTITIGAAACACAGAGAACACCACGAAAAAAGTAACCITGAIGAAGAGGIGAAT 666 67 ACATGTGAACTIATATATTGACACAACCCAGGAGTTGGATATGTGGAAAIAAATTGT 126 568 GCATIGGIGCTAAAAGTITCTIGGAICACATTTITATIAGCIAAAGGGGAAAGTAITACAA 627 247 AAACICICACCICCCAIGITGATCAAAGAACAATATAAAAGAGIGIIAIACCCAITAAI 306 307 GGTTMANCTCGAACACCCAGGNGAGNICAGAACAGAGTGCACGGATAGCAAANAACTA 366 808 GAAAA1GAFACAAGAATTAFTGAAGTTCTCTGTAAAGAACATGAATGTAATATAGATGAG 867 868 GTGAAAAATGTTTGAAAAATTTTATAACGTTTTATGAATTCTCTTGGACTTGTAACA 927 7 ATGICAAGACTGTIGAAGAAGIATGATGTATIGITTGGAALOTICAGAAAITGGAAAGG 66 99.8%; Score 3107; DB 19; Length 3555; 0; Indels 0; Mismatches Pred. No. 0; 100.08: Matches 4107; Conservative st Local Similarity Query Match ŝ ŝ â ŝ 5 Š â ŝ ŝ Ē Ξ $\tilde{\Xi}$

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1048 ATAGANAGTITIGAAANAYAYAGAAAANGIAAAAGIAANGTIGAIGAAGAGGIGAAI 1107
                                                                    1087 PORRARARITHEON PROPERTION OF THE FILL HILLING TO THE TRANSCOTTERN THE
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                                          667 CHAATHOCHCACACACACACTIAGGACTGTIATGAACACIAFCCAAAATAATGAIG 726
                                                                                                                                 727 ATTITAAATDOAGTAATGAALGAAGTTTGAAAAATGTGAITLGGTATTITAAGAAGTGG
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hEST2; telomorase; catalytic subusit, reverse transcriptase; life span; retinoblastoma; p53; tumour suppressor; inhibitor; afterioselerosis; proliferation; immortal; tumour therapy; macular degeneration; activator;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          e.g. the number of mitotic divisions, of a cell. The method relies on activation of a telemerase activity and inhibition of one or both of a retinoblastonm (RD)/INKA pathway or a p53 pathway. Phosphorylation of the by cyclin dependent kinases, cdk4 and cdk6, releases the cells into the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   The invention concerns methods and reagents for extending the life span.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           New method for increasing the proliferative capacity of cell lines
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2827 CCCATTCACCAAAATTATCCTGAACTCTTCTCCAAAAATGGATTATTAGAA
                                      2947 GCTTGTTTTATAAAATTTTGCTTTTAATTAAATAAAAGCTGGAAGCAAAGTTTTAAGT
                                                                                                                                                                                                                                                                                                                                                                        3388 GCTTGTTTAFAAAA111GC1T11AA11AAA1AAAAGCTGGAAGCAAAGTAFAAGCATA
                                                                                                                                                                                                                                                                                                                                                                                                                                          3007 IGATACTATCATACTACTGAAACAGATTTCATACCTCAGAATGTAAAAGAACTTACTGAT
                                                                                                                                                   2887 AAAAATTACTAALTIJACACATTAGAIJIJALTITIANTALTGGAADIJGALATANTGTGT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        3067 TATTTTCTTCATCCAACTTATGTTTTTAAATGAGGATTATTGATAGT 3113
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Claim 5; Page 121-123; 123pp; English.
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                                                                                                                                                                                                                                                                                                                                     AAA29391 standard; DNA; 4839 BP
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Additional constructs include a papilloma virus B7 protein, or other viral one operation which bypasses Rb and/or p53. Antisense constructs of the Rb and p161NK4 appess may also be used. The methods are useful for increasing the proliferative expansity of cells the sells are subsequently of use in pharmaceutical and cosmetic preparations used to treat conditions related to (premature) ageing, e.g. magular degeneration and affections of the vells can also be used to replace tumour cell lines in vitro and for studies on biochemical and physichopical aspects of incoming and differentiation. Long lived (immortal) cells could also be ase in the production of normal or genelically engineered biotechnology products.

059 TCTAATGGACTICCAGAGGITGAAAATCTTTCTAAACGATACGAAGAAATTTATCTTAAA 1118 1179 ATAGACACTITICAAACACACACACACACACAAAACTAACCTTCATCAACACACACCTCAAC 239 GTAATIGGIGGAGAGAGIGGAGIIAAGGAGIGIIAIGAAGAGIATIGGAAGAAITAAIGAIG 1298 1299 ATTITAAATTCAGGAAGTGALCAACGTTCAGAAAATCTGATTTCCTATTTAACAACTGC 1358 487 ICIAAIGGACIICCAGAGGIIGGAAAAICTIITCIAAAACGAIACGAAAGAAAIIIAICIIAAA 546 547 ANTANAMATCTAGATGAAGATTATTTTGGATCATGATAAAACTCTTCAGACTGTTCT 606 607 ATAGACAGTITIGAAACACAGAAACACACGAGAAAAGTAACCITGAIGAAGAGGGGGGAAT 666 979 AIGICAAGACIGIIGAAGAAGTATGATGTATTGTTTGCACTGTTCACGAAATTGGAAAGG 638 67 ACATGIGAACITATATATATTIGACACAACCAGCAGTICGATATCTACTGAAATAAATICT 126 127 GCATTGGTGCTAAAAGTTTCTTGGATCACATTTTTATTAGCTAAAGGGGAAGTATTACAA 186 699 GCATTGGTGGTAAAAGTTTCTTGGATCACATTTTTATTAGCTAAAGGGGAAGTATTAACAA 758 187 ATGGAAGATGATCTGGTGGTTTTCATTTCAGTTAATGCTATGTGTCCTTGACTATTTTTT 246 247 AAACTCTCACCTCCCATGTTGCICAAAGAACCATATAAAACAGCTGTTATACCATTAAT 306 819 AAACTCTCACCTCCCATGTTGCTCAAAGAACCATATAAAACAGCTGTTATACCCATTTAAT 878 879 GGTTCACCTCGAAFAFFFAFGGAGGTFAAAAAGAGGGATAGCAAAACAACTA 938 367 GAAAALGATACAAGAATTATTGAAGTTCTCTGTAAAGAACATGAATGTAATATAGATGAG 426 427 GIGAAAAAIGIIIAITIIGAAAAAITIIAATACCIIIIAIGAAIICICIIGGACIIGIAACA 486 667 GTAATTGCTCCACACACTGCAGIIAGGACIGTTAFGAACACTATGCAACTAATGATG 727 ATLLIAAALTCAGCAAGTGALGAAGCTTGAGAAAATCTGATTTCGTAFTTTAACAACTGC 786 787 ACAGTGAATCCAAAAGAAAGTATACTGAAAAGGAGGAGATATAGGATACATCTTTAAA 846 939 GAAAATGATAGAAGAATTATTGAAGTTCTGTAAAAGAACATGAATGTAATATAGATGAG 998 ? ALGERANANTERANDANTERANDANTER ENGINTER PERONDERANTERINGANDERANDER 56 99.8%; Score 3107; DB 21; Length 4839; 100.0%. Pred. No. 0. Indels Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other; Ö Mismatches Ö 100.0%; onservative. Best Local Similarity Matches 3107; Conserv 8888888888 Ś ŝ Ś £ â Š 3 2 ŝ Ē 3 ŝ Š ŝ Š £ Š Ē ŝ Ē ŝ ä

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2347 AAA GARGA CICAASARTI GOTGGAGACI GIGTACACETERAATI GATGGEGEA 2406
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1927 AGCCTIACAAGIITCCTAGIICACCCTIACGGAITCCTGGAGGGAACAICIAITICA 1986
                                    2407 CAGALGTGACTGTATAACTTTCCCAGGTTCTGTTTATGGCCACATTTAATATCTTCAGCT 2466
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facilitate the development of screening assays to evaluate the potential
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3579 IGATACTATCATACTACTGAAACAGATTICATACTICAGAATGIAAAAGAACTTACTGAT 4648
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Novel androgen receptor associated proteins used to detect androgenic or antiandrogenic activity in screening assays for candidate pharmaceutical molecules which promote or inhibit the activity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                579 ATGTCAAGACTGTTGAAGAAGTATGATGTATTGTTTGCACTCTTCAGCAAAL GGAAAGG 638
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Human; androgen receptor coactivator; ARA54; ARA55; ARA24; detection;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       7 ATGTCAAGACTGITGAAGAAGIAIGAAGIATGIIIIGGA LGIIGAGGAAAIIGGAAAAAG 66
                                                                                                                                                                                                                                                                                                                                                                           Rb; androgenic; antiandrogenic; identification; prostate cancer; ss
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     The present sequence encodes a human androgen receptor coactivator
                                                                                                                                                                                                                                                                                                                  Human androgen receptor coactivator Rb encoding cDNA SBQ 10 NO:7.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      99.8%; Score 3107; DB 21; Longth 4839;
                                         3067 TATTTTCTTCAFCCAACTTATGTTTTTAAATGAGGTTAFTGATAGT 3113
                                                             3639 TATITICITCATCCAACTIATGITITIAAATGAGAATTATTGATAGT 4685
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Znote= "androgen receptor coactivator"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       efficacy of drugs in the treatment of prostate cancer.
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                                                                                                                                                                                       AA288444 standard; cDNA; 4839 HP
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7	A FORMACH TATATETGACACAGCAGCAGTTCGATATCTACTGAAATAAAT	869	
127	TGGTGCTAAAAGTTCTTGAATCACTTTTATTAGC 	186 758	
7.87	GATTETCATTECAGTEAATGCTAUGIGCCTTGACTATETT 	246 818	
247 813	VTGTCN/YGTGGGATGTGGTGAAAGAAGGATATAAAAAGAGTGTTATAGGGATTAATAA	306 878	
£13 £13		366 938	
7.43	GAAAATGA FAGAAGAATTATTGAAGTTGTGTAAAAGAAGATGAGTGTAATATAGATGAG ETELELELELELELELELELELELELELELELELELELE	126 998	
444	GIGAAAAALGITTALTICAAAAAITTIAIACCITTIAIGAATICICTIGGACTIGIAACA FILLILILILILILILILILILILILILILILILILILI	486 1058	
487 1.59	TCTAATGGACTTCCAGAGGTTGAAAATCTTTCTAAACGATACGAAGAAAATTTALCTTAAA 	546 1118	
547 1119	1101 1111	606 1178	
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1239	GTAATTCCTCCACACACTCCASTTAGGACTGTTATGAACACTATCCAACAATTAATGATG 	7.26 1298	
727	ATTELAAATICACCAACUGARCAACCUFCAGAAATCUGATTUCCTATTTTAACAACUGC 	786 1358	
787	ACAGTGAATCCAAAAGAAAGHTATACTGAAAAGAGTGAAGGATATAGGATACACATGTTAAA 	846 1418	
н47 1419	TIGGIAAAGGIGIGGGACAGGGITGIGIGGAAATIGGATCACAGGATACA - - - - - - - - - - - - - - - - - - -	906 1478	
307 1479	ACGA HTTI ACGA	966 1538	
367 1539	ITCAAAATTTTAGGAAACTICTGAATGACAACATTTTCATATGTCFFHATTG 	1026 1598	
1027 1569	GERGEGETEGREGETEGTAATGGCCACAATAGCAGAAGGTACATCATGAT 	08 65	
1659 1659	AATTEGECTTECCATGGATTCTGAATGTGCTTAATTTAAAAGCCTTTGAT 	1146 1718	
1147	IIITACAAAGIGAIGGAAAGIIITAICAAAGAGAGAGGA 	1206	

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2139 CGCCTTCTGTCTGAGCACCASAATTASAACATATCATCTGGAGGCCTTTTCCAGGACACC
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                                                                                      1267 CCTTTATTTGALCTTAFTAAGAATGAAAGGAGGAGAAGGAGGAGGAGGAGGAGTGAA
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                                                                                                                                                                                              TCTCCTGTAAGATCTCCAAAGAAAAAGGTTCAACTAGGGTGTAAATTCTAGTGGAAAT
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Human, cancer; colon; breast; ovary; acsophagus; kidney; thyreid;
stomach; hung, prostate, puncreas; carcinoma; antitumour; cancerous;
cytostatic, que therapy; antineoplastic; Wilm's tumour; adenocarcinoma;
                                         2287 CGAACACGAALGCAAAAGAAAAAAGALGALAGCATGGALAGCTGAAAGAAGAAGAAGA 2346
                                                                                                                                                       2.447 AAATGAGGATCTCAGGACCTTGGTGGACACTGTGTACAACTCTGGATTCATTGTCTCA 2406
                                                                                                                                                                                            A MARKING FAGARI GRAND GAT BANGCAGGGT GTRETA ANTI TI GRETTETTE 12706
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The present invention describes a method (ML) for screening for an auti-neoplastic agent. The method involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, determining a change in comprises a sequence (S) selected from B47 sequences (H) comprises a sequence (S) selected from B47 sequences (H) where a change in to ABC70110), or is at least 95% identical to (S), where a change in expression is indicative of anti-neoplastic activity. (I) has eyrostatic activity and can be used in gene therapy. MI can be used for screening an anti-neoplastic agent, and can be used for producing a product which is the data collected with respect to the anti-neoplastic agent as a

Homo sapiens

Carter KC, Ebner R, Endress G, Horrigan S;

Augustus M, Weaver Z;

Soppet DR, Young PE,

WPI; 2002-188264/24.

chemical agent to be tested for anti neoplastic activity, and determining a change in expression of a gene of a signature gene set Screening for anti-neoplastic agent involves exposing cells to a

Claim 1; SEQ 1D 1210; 44pp; English.

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result of M1, and the data is sufficient to convey the chemical structure and/of properties of the adent. M1 can be used in the refunct of cancer such as colon, breast, stomach, lung, thyroid, besophageal, ovarian, Kidney, prostate or pancreatic cancer, adentocarchoma, carchoma, clear cell cancer, infiltrating ductal cancer, squamous cell carcinoma, neuroendocrine
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0 999 GIGAAAAAIGTITATITICAAAAATITITATACCTITITATGAATITCICTIGGACTIGTAACA 1058 1119 AATAAAGATOTAGATGGAAGATTATTTTTGGATGATAAAAAGTGTTTGAGAGTGATTGT 1178 .239 GTAATTGGTGGAGAGAGTGGAGTTAGGAGTGTTATGAACAGTATGGAGAATTAATGATG 1298 1359 ACAGIGAATGCAAAAGAAAGTAFACTGAAAAGAGTGAAGGATATAGGATACAFCFTTAAA 1418 187 ATOGAAGA EGATICTIGGTGATTTTGAGTTPAATGCTATGTGCTTGAGTTGAGTATTTTATT 246 427 GIGAAAAAIGTITATICAAAAATTITATACCIIIIAIGAAIICICIIGGACIIGIAAAA 486 487 ICIAAIGGACTICCAGAGGTTGAAAATCTTTCTAAACGATACGAAGAATTTATCTTAAA 546 607 AIAGACATITIGAAACACAGAAAAAAAAAAAAAASIAAACITIGAIGAAGAAGII 666 KEZ BLAALLOPPOPACACAPPOPACTTAGGACTGTTATGAACACTATCCAACAATTAATGATG 726 7.27 ATH HAAAFI CAGCAAGEGAEGETCAAAAATCEGATEFECETAFFFFAAAACTGC 786 67 ACATGTGAACTTATATATTTGALACAACAGGAGTICGAIATCIACTGAAAIAAATICI 126 127 GOATTOOTGCTAAAAGTITCTFGGATCACATTTFFAFFAGGFFAAAGGGGAAGTAFFACAA 186 247 AAACTCTCACCTCCCAIGTIGCTCAAAGAACCAIATAAAAACAGCTGTTAIACCCATTAAT 306 467 GAAAAIGAIACAAGAATTATTAAAGTTTGTGTAAAGAAGATGTAATGTAATAGAGGA 426 787 ACAGTGAATCCAAAAAAAAGTATACTGAAAAAGAGTGAAGGATATAGGATACATCTTTAAA 846 847 GAGAAATITIGGTAAAAQCITGTGGGACAGGGTIGGTGTGGAAATITGGATGAGAGGGATACAAA 906 0; Gaps 7 ALGICAAGACIGTIGAAGAAGTATGATGTATTGTTTGCACTCTTCAGCAAATTGGAAAGG 66 Score 3107; DB 24; Length 4839; Pred. No. 0; Indels Sequence 4839 HP: 1534 A: 902 C: 880 G: 1523 T: 0 other: carcinoma, papillary carcinoma and Wilm's tumour. 0; Mismatches 100.0%; 388.66 Conservative tocal Similarity Matches 4107; 1 5 2 Š ŝ 2 5 Ē \geq 3 ŝ 5 ŝ

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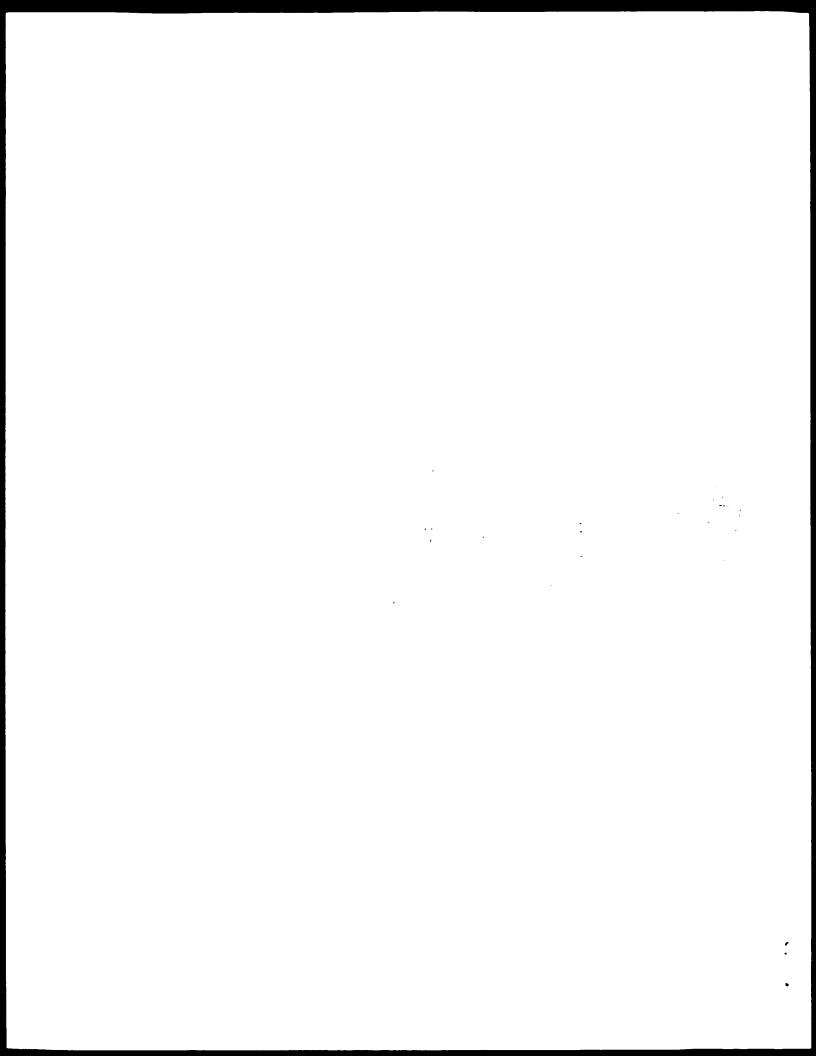
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Diagnosis of retinoblastoma - using genetic material corresp. to a normal
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Copyright (c) 1993 - 2003 Compugen Ltd.
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This sequence encodes a modified relinchastome tumour suppressor protein (RISP) of the invention. The proteins can be used for inhibiting collular proliferation, when coadministrated with a psa protein. The PISBs out to used for treating diseases characterised by abnormal cellular proliteration, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
                                                                                                                                                                                                                                            Kerin blastoma suppressor protein with N-terminal modification - inhibiting cellular proliferation, particularly cancel
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P.ESER, AAW69376.
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Sequence 3554 BP; 1170 A; 683 C; 653 G; 1048 T; 0 other;

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27. DF	281	HisGluCysAspileAspcluVallysAspValTyrPhcLysAspPtclicFroPheMet 300
ογ Op	301 907	AsnSerLeuGlyLeuValThrSerAsnGlyLeuProGluValGluAsnLeuSerLysArg +20
ςς Cp	321 967	TyrGluGlufleTyrLeuLysAsnLysAspLeuAspAlaArgLeuPheLeuAspHisAsp 440
.t. 6	34:	LGSTARLUGULTBIASESCITTCASESCIPLOGLUBITSTAANGRITTOARGESSKY 360
oy Op	361 1087	AsnLeuAspGludluValAsnVallleProProHisThrProValArgThrValMetAsn 380
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oy Op	481	IlePheHisMetSerLeuLeuAlaCysAlaLeuGluValValMetAlaThrTyrSerAra 500
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The sequence is that of the retinoblastoma gene which encodes the retinoblastoma (RB) protein which may be used as part of a method of controlling cell cycle progression which may be used in combination with therapeutic methods to arrest tumour decreases in organisms. The cell cycle can be reversibly arrested in a convenient and sate.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         manner. The protein is used in a compan, is relatively inexpensive and readily obtainable, and shows little or no toxic effects on healthy cells. It is also compatible with other methods and devices for regulating certain physiological processes of the body, such as blood cell produ, and gamete produ. Fraqments of the protein are soluble in low conens, of alycerol thus enhancing their value in
                                                                                                                                                                                                                                                                   KM dene product; p56KM portion; cell cycle progression control; combination; therapeutic methods; arrest; tumouriquesis; regulation; physiological processes; blood cell produc:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Method of controlling cell cycle progression – uses purified retinoblastoma protein or fragment, for use in combination with therapeutic methods to arrest tumoriquesis
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Matches:
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/note- "Rb protein"
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                                                         Disclosure, Fig 9; 68pp; English.
                                                                                                                                                  AAQ41545 standard; DNA; 2994 BP.
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                                                                                                                                                                                                                                       Retinoblastoma gene.
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Best Local Similarity:
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Belinoblastoma protein RM: BZF; transcription lactor, homan,
bladder cancer: restenosis; andioplasty; diabetic retinopathy;
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peripheral vascular disease; therapy; ss.
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22 MAY 1998.

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This nucleotide sequence includes a coding region for retinoblastoma protein RB (see AAM62465). A new claimed polypoptide is a fusion of: (i) a transcription lactor (TP) comprising a DNA binding domain, and (ii) a retinoblastema (Rb) polypoptide that includes a growth suppression domain. Also new are: (i) a nucleic acid emoding the fusion protein, and (2) expression vectors containing such DNA. The fusion protein, particularly expressed from gene therapy
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   81 ValSerSerValAspGlyValLenGlyClyTyr:14cOntysLynClyGGGAAcolTrpCly 100
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               transcription of the E2F promoter than Rb alone and cause cell-cycle
                                                                                                                                                                                                                                                                                                                                                                                                                                                                              vectors (especially adenovirus vectors), is used to treat theyeproliterative conditions, specialisty cancer (particularly of the bladder) or restencists (after analoplasty), but also diabetic retinopathy, thyroid hyperplasia, Grave's disease, psoriasis, bring prostatic hypertrophy. In Francen syndrome and peripheral vascular disease. Tissue specific expression of E2F MR tustoms is provided. The fusion proteins are more effective in repressing
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       61 CysClnLysLeuLysTleProAspRisValArqGluArqAlaTrpLeuThrTrpGluLys
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                                                                                                                                                                                                                              New fusion polypoptide of, e.g. transcription facto; use treat, e.g. hyper-proliferative disease such as cancer and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Sequence 2994 BP, 974 A; 618 C; 593 G; 809 T; 0 other;
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Conservative:
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                                                                                                                                 Antelman D, Gregory RJ, Wills KN;
                                                                                                                                                                                                                                                                                                      Example 1; Fiq 2A; 91pp; English.
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97WO-US21821.
                                    97US-0801092.
96US-0751517.
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                                                                                            (CANJ-) CANJI INC.
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                                                                                                                                                                                       P-PSDB; AAW62465.
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13 · NOV - 1997;
                                    14-FEB-1997;
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Oy Ob	841	ThrserdlubysPhedlobysTicAsnchmetvalcysAsnsorAspAraValberbys 860 111111111111111111111111111111111111

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tool for diagnostic retinoblastoma. Rh eDNA or genomic DNA are preferably waved as probes to determine the detect region of the mRB gene through genomic DNA blotting analysis or using the method of restriction tragment length polymorphism analysis to determine the diseased allele. Glored RB enth can be used to generate specific anti-RB protein (anti-ppRBIB) and thooless which are useful immunoscretering of tissue biopsy. The diagnostic method is particularly intended for use in screening
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           RM gene; human; retinoblastoma gene; mutation detection; immunoscreening; retinoblastoma diagnosis; hereditary retinoblastoma; secondary cancer; esteosarcoma; glioblastoma; breast cancer; lumentiquenesis suppression; sa
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            The invention relates to a method of detecting a mutated retinoblastoma (minth) merbic acid in mannals comprising hybridizing an isolated that length, wild type MF WIKH) for probe to a cell sample and detecting a mutated RH nursicle acid. The method is useful as a diagnostic
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 cancer, such as, ostrosarcoma, fibrosarcoma, glioblastoma, breast cancer whether or not connected with retinoblastoma. The method is also used in the suppression of fullouding-resis where the absent RB protein ppRRHIO will be provided through the molecular induction and quier transplanting of the RB cDNA to the individual in need of ppRBHIO.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      families with a history of hereditary refinchlastoma and for screening their children. It may also be used in prophylactic and postnatal screening and for the prediction of the development of secondary
                                                                          861 ArdSerAlaGludlySerAssProProLysProLeatySLysLeuArgPheAspIleGlu 880
                                                                                                                                                           901 LenAladluMetThrSerThrArgThrArgMetGlnLysGlnLysMetAsnAspSerMet, 920
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241 ThralaValileProileAsiGlySerFrcAidThrFrcAidArdGlyChnAshArdGer 260
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779 GGAT.ASATGAAGCAGATGGAASTAAACATTTCCAGAGAGTCCAAATTTCAGCAGAAA 2838
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                                                                                                         821 Thr ProThilysMetThr ProArgSet ArgileLeuvalSerlleGlyGluSerPheGly 840
41 ArgValLeulleLysSiusluslusluTyrAspSerIleIleValPheTyrAsnSerValPhe 760
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Human pilu-KB retinoblastoma tumour suppressor encoding cDNA.
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Recombinant adenoviral vectors useful for gene therapy of cancer, especially p53 deficient tamours
     /Product = "plio PM"
/product = "plio PM"
/hoto: "retinoblastoma fumour suppressor"
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                                                                                                                                                                                 Disclosure: Fig 3: 50pp: English.
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the present invention describes a composition comprising a recombinant ademovirus expression vector, where the vector has an insert of excapance Long comprising a game encoding a forting mand protein and ademovirus DNA in which all of the coding sequences of Elb, Elb, and protein iX, and part of E3 are deleted. The vectors are useful in gene therapy frequencing of cancer, especially for treating p53 deficient tumnours. The vector enables safer and more efficient gene therapy of cancer. The present sequence encodes human p110-RB refinoblastoma bunour suppressor which can be used as the foreign gene in the above

Sequence 2995 BB; 975 A; 618 C; 593 G; 809 T; 0 other;

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٠. د ۲	7.1	ProAlaProProF	ordordordor	31uGluAspProGluG	ProAlaProProProProProGluGluAspProGluGluAspSerGlyProGlu	4
ą Ž	199			IIIIIIIIIIIIIIII SAGGAGGAGGGAGAGG	CHARLES CONTROLLES CON	1.4
7.7	4		alArqLeuGluPhe	3luGluThrGluGluP	AspteuProteuValArqteuGluPheGluGluThrGluGluProAspPheThrAlaLeu	4
qq	6,1,7	0 V 0CTGGGTGTGG	TCAGGCTTGAGTTTC	BAAGAAACAGAAGAAC	GACTGCCICTCTCTCTCTTTGAAGAACAGAACAACCTGATTTACTGCATTA	
0.7	1,		ysileProAspHisV	ValArgGluArgAlaT	CysGlnLysLeulysTleProAspHisValArgGluArgAlaTrpLeuThrirpGluLys	J.
40	41.9	TGTCAGAAATTAA	AGATACCAGATCATC	GTCAGAGAGAGAGCTT	TGTCAGAAATTAAAGATGCAGATCATGTCAGAGAGAGAGA	
٠ د ۲	r r		(SpGlyValLengly)	SlyTyrileGlnLyst	Valser SerValAsptiyValLeuGlyGlyTyrIleGlnLysLysCluLeuTrpGly	
ą.	473		ALGGAGIALIOGGAC	GGTTATTTCAAAAGA.	GTTTCATCTGGATGGAGGAGGAGGGAGGGAGGAGAGAAAAGAAAAGAAAAGGGG	4
65	101		HeCysHePhelleAlaAlaValAspLeu	LeuGlyAspMetSerP	11-0"ys11-0Phe11eAlaAlaValAspLeuGlyAspWetSerPheThrBheThrGhuLeu 	_

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qq	439	ATCTGTATCTTTATTGCAGCAGTTGACCTAGAGATGTCGTTCGT
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7 <u>Q</u>	499	
ò	141	SerThrivsValAspAsnAlaMetSerArgLeulvsLvsTvrAspValLeupheAla 160
<u>q</u>	559	
Oy	161	LeupheSertysLeuGluArqThrCysGluLeuTleTyrLeuThrGluProSerSerSerTB0
qq	619	CTCTTCAGCAAATTGGAAAGGACATGTGAACTIAIATTTTGACACAAACTAGCAGTTCG 678
Óγ	181	HeSerThrGluileAshSerAlaLeuValleuliysValSerTrpHeThrPheteuleu 200
qu	619	ATATOTACTGAAATAAATICTGCATTGCTGCTAAAAGTTCTTGGATCACATTTTTATTA 738
ò	201	AlaLysolyGluValLeuGlnMetGluAspAspLeuVallleSerPhechhileuMetLeu 220
q 0	739	GCTAAAGGGGAAGTATTACAAATGGAAGATGATTTTTTTT
0.7	22.	CysVallouAsp77 Pbc/JelysbeugerTreProMetiaglaabysGlabou77 bys 240
qq	799	TGTGTCCTTGATTTTATTAAACTCTCACCTCCATGTTGCTCAAAGAACCATATAAA B58
Οy	241	ThratavallleprolleasnGlySerProargThrProargatgGlyGlnasnatqSer_260
qq	859	ACAGCTGTTATACCCATTAATGGTFCACCTCGAACACCCAGGCGAGGTCAGAACAGAA
λ 	261	AlaArgileAlaLysGloteuGluAsnAspThrArgile?leGloValLeurysLysGlu 280
qu	616	OCACGGATAGCAAAACAACTAGAAAATGATACAAGAATTATTGAAGTTCTCTGTAAAGAA 978
O.	281	HisGluCysAsnilcAspGluVailtysAsnValTyrPhetysAsnPhetteProPheMet. 300
40 ;	979	CATGAATGTAATATAGATGAGGGGAAAAATGTTTATTCAAAAATTTTATAGCTTTTATG 1038
0y	301	AsnSerLeuGlyLeuValThrSerAsnGlyLeuProGluValGluAsnLeuSerLysArq 320
00	1044	ANTICTOTOTOTOTOTOTOTOTOTOTOTOTOTOTOTOTOTOT
20	321	TyrcluclutleTyrLeuLysAscLysAspLeuAspAlaArqLeuFletzeAspHisAsp 440
10 b	1099	PACGAAGAAATITAICITAAAAATAAAGAICIAGAIGCAAGAITAIIITIGGAIGAI 1158
δλ	341	LysThrieuGinThrAspSerTieAspSerTheGhuThrCluArqthrProArqtysSer 360
QQ	1159	AAAACTCTTCAGACTGATTCTATAGACAGTTTTGAAACACAGAGAACACACGAGAAAAAGT 1218
Οy	361	AshLeuAspCluGluValAsnVallleProProBisthrProValArqthrValMetAsh 480
106	1219	AACCITGATGAAGAGGTGAATGTAATTCCTCCACACTCCAGTTAGAACTGTTATGAACT 1278
ζ	381	ThrileGindinLeuMetMetIleLeuAsuSerAlaSerAspdinProSerGinAsuLeu 400
Ob	1279	ACTATCCAACAATTAATGATGTTTTAAATTCAGGAAGTGATGAACTTTAGAAAATTG 1338
ΟŸ	401	Heseryribeashashgystbrvatashgyschasertletentysatayattys 420
qq	1339	ATTICITATITAACAACIGAACAGGAGAACAAAAGAAAGTATACIGAAAAGAAGAAGTAAAAGAAAGAAAGAAAGAAAGAAAGA
òγ	421	ASPITECTYTYTHER PROBLESS PROATETS SATAVATOLYCHETY FOR THE
qc	1349	GATATAGGATACATCTTTAAAGAGAAATTTGCTAAAGTTGTGTGTG
o,	441	lledlyserdlmArqTyrLysLeaGlyValAraLouTyrTyrAraValMerGluserMer 460
0.0	1454	AFTOGATOACAACAACATIGAACTIGGAGIIGGATIGAATIACOGAATAATGGAATAATAATAATAATAATAATAATAATAATA
ΟŊ	461	LeulysSerG uG uG uGrg .cuSerHeG nAsnrheSerIysLeuLcuAsnAspAsn 480
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11.7. ALTHUR HILLIH HIL
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           1939 TIAATIIAAAAGCCIIIGATITITACAAAGTGATCGAAAGTITIAICAAAGCAGAGGC 1758
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                           821 ThrProThrLysMetThrProArgSerArg11eLeuValSerTleGlyGluSerPheGly 840
481 IlePheHisMet.SerLeuLeuAlaCysAlaLeuGluValValWalMetAlaThrTyrSerArg
                                                                                                                                                                                                                                                                                                         101 SerThrSerGlnAsnLeuAspSerGlyThrAspLeuSerPheProTrpIleLeuAsnVal
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comprising a deletion in the protein IX gene and a gene encoding a forcign protein. This vector can be used in gene therapy, particularly throduce tumoun suppressor genes into cancerous cells. Genes which may be used include F23, thymiline kinase and retinoblastoma tumour suppressor gene (Rb). The present sequence is the retinoblastoma tumour
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Recombinant adenovirus expression vector comprising a partial or total deletion of a protein IX DNA and a gene encoding a toreign protein e.g. suicide protein, useful for inhibiting or reducing the proliferation of
2779 GGATCAGATGAAGCAGATGGAAGTAAACAICICCCAGGAGAGTCCCAAATTICAGCAGAAA 2838
                                                                                                                                                                                                                          861 ArgSerAlaCluClySerAsnProProLysPreLeulysLysLeuArgPheAsplleClu 380
                                                                                                                             981 C!yScrAspC!cAlaAspC!yScrIysRisi.cuir.cCiyC!uScrIysPheGlnGlnthiys 900
                                                                                  901 LeualaGlumetIhrSerThrArgThrArgMetGlnLysGlnLysMetAsnAspSerMet
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    The present invention describes an adenoviral expression vector
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Retinoblastoma; tumour suppressor protein; Rb; p53; cancer;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Sequence 2995 HP; 975 A; 618 C; 593 G; 809 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     adenoviral vector, gene therapy, thymidine kinase, ds.
                                                                                                                                                                                                                                                                                                                                                                                                                                                     Retinoblastoma tumour suppressor gene.
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                                                                                                                                                                                                                                                                            2899 GATACCTCAAACAAGGAAGAAAA 2922
                                                                                                                                                                                                                                                          921 AspThrScrAsnLysCluCluLys 928
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characterised by the partial corteral deletion of the adenoviral protein to TN NAM Expression and a foreign protein of the adenoviral protein having a gene encoding a foreign protein when as tumour suppressor protein, pl10RB (retlinoblastoma) and p53. Adenovirus vector is used protein, pl10RB (retlinoblastoma) and p53. Adenovirus vector is used in spraticularly useful for treating uniour suppressor genes useful in gene therapy. The vector is particularly useful for treating useful for treating useful for treating the protein such as thyroid hyperplasia, Grave's disease, psoriasis, hepatocellular carbinoma, neophlasms, leukaemias, lymptomas, etc. to inhibit tumour proliferation or to ameliorate particular related and bathology such as slocks cell anaemia and Tay-Sachs disease. The vector is also useful for the safe tecombinant production of diagnostic and therapeutic polypeptides and proteins.
                                                                                                                                                                                                                                                                                                                                  New recombinant adenovirus expression vector having a gene encoding for a foreign profein and a partial or total deletion of the adenoviral profein IX DNA, useful in gene therapy for treating or reducing
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The lowering expression rector
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Mismatches:
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                  1519 CLIAAATGAGAAGAAGATTALGGALTGAAAATTTAGGAAATTTG GAALGACAAC
                                                                      2179 TGGACCTTTTCCAGCACACCCTGCAGAATGAGTATGAACTCATGAGAGACAATTTG 2248
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Retinoblastoma; tumour suppressor protein, p110-KR, cell cycle, p53,
Kb; mitosin; cell death; adenoviral protein IX; gene therapy; cytostatic;
eleveritys cypression recter; tumour; non-small cell lung cuncer;
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melanoma; retinoblastoma; colorectal carcinoma; sarcoma; Wiln's tumbou;
astrocytoma, qliobiastoma; neuroblastoma; ovarian carcinoma;
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                                                                                                                              2599 ACACCANTAAAAATGACTCCAAGATCAAGAATCTTAGTATCAATTGGAATGATTGGGG 2658
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                                    84] ThrSerGlufysPheClnfysTleAsnClnMetValCysAsnSerAspArgValfeutys 860
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                                                                                                                                                                                  *** ** TecraspolualaAspolySortysHisLogProOlyGluSertysPheClnGladys
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  asoful in gene therapy, particularly for treating or suppressing
                                                                                                                                                                                                     And he have ment to appropriate protection of the PB periodist and Andrews
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   osteosarcema; renal cancer; gene, ss.
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Disclosure; Fig 3; 37pp; English.

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The present invention describes a recombinant adenovirus expression vector, which comprises a partial or total deletion of a protein IX DNA and a given excepting fretein. The recombinant adenovirus vector can have expression rector is particularly useful for treating or suppressing proliferation of a tumour, e.g. non-small cell lung cancer, small cell lung cancer, small cell lung cancer, small cell lung cancer, breater tumour, bladder tumour, colorectal carcinoma, sarroma, prostate tumour, bladder tumour, colorectal carcinoma, sarroma, tissues, Wilm's tumour, astrocytoma, glioblastoma, neuroblastoma, colorectal carcinoma, colorectal carcinoma, sarroma tissues, Wilm's tumour, astrocytoma glioblastoma, neuroblastoma, osteosationa of texal cancer. The present sequence encodes the retinoblastoma tumour suppressor protein pilo-RB, which is
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      121 Clnt.gsAsnilcCluffeSerValHistgsPhePheAsnicuLcatgsGluffeAsplhr 140
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protein (RISB) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The PISPs can be used for treating diseases characterised by abnormal cellular.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Notinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Sequence 4555 BP; 1171 A; 684 C; 653 G; 1047 T; 0 other;
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                                            Modified retinoblastoma tumour suppressor gene.
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101 IleCysIlePheIleAlaAlaValAspLeuGlyAspMet.SerPheThrPheThrGluLeu 120
                                                                                                                                                                                                                                                            161 LeuPheSerLysLeuGlaArqThrCysGluLeaIleTyrLeuThrGlaFroSerSerSer 180
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2467 ACMOGNACAAAAAIGACTOGNACAAGAACTHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
                                                                        901 TonalaGTuMetThrserThrarqThrarqMetGLnLysSTBLysMetAsBaspScrMet 920
                                           861 ArgSerAlaGluGlySerAshProProLysProLeuLysLysLeuArqPheAsp11eGlu 880
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        The present sequence appears in the specification, which describes a tetracycline responsive expression vector (TKEV), which contains a sequence encoding a fusion protein comparison of a transcriptional transactivation domain (TTD) operatively attached to a totracycline repressor protein (TKE), the first sequence operatively positioned downstream of a promoter. The vector also contains a clouing site operatively positioned downstream of a basel positioned downstream of a basel positioned as
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Minimal promoter; tetracycline responsive expression vector; TREV;
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lightly controlled expression of genes, such as tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   transcriptional transactivation domain; IID;
tertacycline repressor protein; TRP; Tetracycline operator;
production, stable cell line, protein production;
tumour suppressor protein; treatment; cancer; ss.
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The strangeline operator. The Hews can be used to produce stable cell inse in which done operator. The striping required by the straing stable as the stable december of the production of proteins such as thouse. XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	Seion is tightly regulated by tetracycline. Production of profeins such as tumour can be used for freating diseases character Heration, particularly cancers. 684 C; 653 G; 1047 T; 0 other; Matches: 926 Conservative: 1 Mismatches: 0 Gaps: 0 Gaps: 0	0 10 0 0 0	~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	ValhistysPhePheAsniculculysGlullcAspthr 140	0 0 0 0 - 0 0
racycline costs which costs which contine about a line and a line	pperator. The IREMS can be used of dene expression is tightly relead for the production of protections which can be used for training which can be used for training proliferation, particularly 1171 A; 684 C; 653 G; 1047 B; 1171 A; 684 C; 653 G; 1047 B; 1171 A; 684 C; 653 G; 1047 B; 1077 B; 1040 B; 1040 B; 105 B; 1040 B; 105 B; 10	1-928) x AAV54990 (1-3555) stysthrProArdtysthrAlaAlaThrAla MAAACCCCCGAAAAAA GGGGGGGGGGGGGGGGGGGGGGG	CTCGTCACGTTGACTTGACATACAGAACAGAA ILCUIYS CPPCOASPHISVALAFGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG		GluffeasnSeralateuValleutysVal GaaataaattetGeattGGTGCTaaaGtT GluValLeuGlbMetGluAspaspfeuVal HILLIHHIHHHHHHHHHHHHHH GaagtaltacaaatGaagatGTCGTG AspfyrfacletgcLecserPreFroMet HHHHHHHHHHHHHHHHHHH GactattataaatGTGCACGTGATG
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O.Y.	301 907	AshSertenClytenValThrScrashClytenFreQluValCluAshLenGertysAtg *20
9. 0.	321	TyrdludlutletyrLeuLysAspLysAspLeuAspAlaArqLeuPheLeuAspHlsAsp (40
Q.Y.	341	LysthficugInthraspserileaspserbhegluthrGinargThrproardlyssor 460
ΟΥ	361 1087	AshleuAspGluGlüValAshVallleProProRisThrProValArgThrValMetAsh 380
Qy qu	381	ThrileginginLeuMetMetileLeuAsnSerAlaSerAspGinProSerGluAsnLeu 400
QY	401	POSOTTYTPHOASEASINGYSTHTVALASEBTOLYSSUBSETHELGULYSATGVALLYS 420
cy ob	421	ASETICOLYTYTIICECECTYSCIULYSPHOATSTYSATSVOLOTYCIUGLYCYSVALGIU 440
Qy Db	441	11eSlySerClnArgTyrLysLeuSlyValArgLeuTyrTyrArgValMetGluSerMet. 460
Qy Db	461	LoulysSerGluGluGludrgLeuSerlleGlnAsnPheSerLysLeuLouAsnAspAsn 480
ΟΥ Ob	1447	TephenisMetSerLeuLeuAlaCysAlaLeuGluValValMetAlaTh:TyrSerArg 500
φα Λδ	501	SerThrSerGlnAsnLeuAspSerGlyThrAspLeuSerPheProTrpIleLeuAsnVal 520
Qy Db	521	LebasniculysalarbeaspPheTyrtysVallicCluserPhetletysalacludly 510
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Qy Db	601 1807	ThralaalaAspwetTyrLeuSerPreValArgSerProLysLysLysClysErThribr 620
Qy DD	621 1867	621 ArdValAsnSerThrAlaAsnAlaGluThrGlnAlaThrSerAlaPheClnThrGlbEys 640 411111111111111111111111111111111111

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retinoblastoma; p54; tumour suppressor; inhibitor; arteriosclerosis; proliferation; immortal; tumour therapy; macular degeneration; activator;
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                     TELLITELLE LETTELLE LETTELLE LETTELLE LETTELLE LETTELLE LETTELLE LETTELLE LETTELLE LETTELLE 2646
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641 ProLeulysserThrserLeuserLeuPheTyrLysLysValTyrArqLeuAlaTyrLeu 660
                                                                                       661 ArquanAsnibitenCysGluArquanLeuSerGluHisProGluLeuGluHisFlettle 680
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treat conditions related to (premature) ageing, e.g. machlar degeneration
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       The invention concerns methods and readents for extending the life-span, e.g. the number of mitoric divisions, of a cell. The method relies on activation of a telemerase activity and inhibition of one or both of a retinoblastoma (Rb)/INR4 pathway or a p53 bathway thosphorylation of Rb by cyclin-dependent kinsses, c4k4 and c4k6, releases the cells into the division cycle. Binding of INR4 lamily members, e.g., the tumour suppressor placing of inhibits kinase activity and results in growth arrest. Rb inactivators can selectively and reversibly inactivate an Rb/INR4 pathway, especially an Rb/Pl6:NR4a pathway. The encoprotein NDM2 is a cellular inhibitor of Rb/EEF function and the p53 timour suppressor.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     lines in vitro and for studies on biochemical and physiological aspects of growth and differentiation. Long lived (immortal) cells could also be
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               and can also be used in the methods, other molecules which can be used include cdk4 or cdk6 mutants. In particular, a cdk4 mutant is one which differs from at case or mote of residues E22, E24, E34, E34 and/or D97. Additional constructs include a papilloma Virus E2 protein, or other vira! oneogratein which Expasses E0 and/or P64. Antisense constructs of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       increasing the proliferative capacity of cells. The cells are subsequently of use in pharmaceutical and cosmetic preparations used to
                                                                                                                                                                                                                                                                                                                                                                                                                    comprises administering agents reversibly activating recommense activity and reversibly idactivating ALCIAN and Gerpsthays useful
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 and arteriosclerosis. The cells can also be used to replace tumour cell
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 the Rb and pl61NK4a genes may also be used. The methods are useful for
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     1 Met Proprolyst hr ProArglysThrAlaAlaThrAlaAlaAlaAlaAlaAlaAlaBlaCluPro 20
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                                                                                                                                                                                                                                                                                                                                                                                                 New method for increasing the proliferative capacity of cell lines
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    of use in the production of normal or genetically engineered
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 L; 0 other;
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Mismatches:
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Claim 5; Puge 121-124; 123pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                      in treating age related diseases
                                                                                                                                                                                    980S-0109891,
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                                                                                                                                                                                                                                                         (GENE-) GENETICA INC
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                                         WO200031238-A2.
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Homo sapiens.
                                                                                                                                     24 - NOV - 1999;
                                                                                                                                                                                 25-NOV-1998;
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41 AspleuProLeuValArqLeuGluPheGluSluThrGluGluProAspPhrThrAlaLeu 60

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418 IGTOAGAAAITAAGATAGAATGATGATGATAAAAAAGAGGTTAGTTA
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25.08 GGAGGAACATCIATATTIACCCTGAAGAGTCCATATAAAATTCAGAAGGTCTGCCA 2597
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                                                                                                                                                                                                                                                                                                                             2598 ACACCAACAAAAIGACECAAGAIGAAGAIFEIIAGITAGIAITGAATIGGIGAATGAITGGG 2657
                                                                                                                                                                                                                                                                             Novel androgen receptor associated proteins used to detect androgenie or antiandrogenie activity in screening assays for candidate pharmaceutical molecules which promote or inhibit the activity -
781 ProlleProHistleProArqSerProTyrLysPheProSerSerProLeuArq11ePro 800
                                                            801 GlydlyAsnllefyrlleSerProLeulysSerProTyrtysTleSerCluGlyLeuPro 820
                                                                                                                       821 ThrProThrLysMetThrProArgSerArgIleCouValSerIleGlyGluSerPheGly 840
                                                                                                                                                                                   841 ThrserolutysPheclaty=TleAsacleMe(VilCysAsuSerAspArgValLeutys 860
                                                                                                                                                                                                                                                861 ArgSetAlaGluGlySetAsuProProtysProteutgstyst.euArgPbcAspf1cClu 880
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Rb; androquence; antiandroqueic; identification; prostate cancer; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Human androgen receptor coactivator Rb encoding conA 3110 to NO.7.
                                                                                                                                                                                                    Znote- "androgen receptor coactivator"
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of androgen receptor co-activators such as those of the invention will facilitate the development of screening assays to evaluate the potential
                                              designated Rb. Androgen receptor co-activator profelts from the present invention can be used in serrenthal assays to identify candidate pharmaceutical molecules for the ability to promote or inhibit the interaction of androgen receptors and androgen responsis e elements to modulate androgenic activity. The identification and characterisation
                                                                                                                                                                                                                                                                                                                                                                                                              417
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                                The present sequence encodes a human androgen receptor coactivator
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                                                                                                                                                                efficacy of drugs in the treatment of prostate cancer.
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Mismatches:
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Claim 8; Page 47-53; 59pp; English.
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241 ThrAlaVallleProlleAsnGlySerProArqThrProArqArqGlyGlnAsnArqSer 260

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251 AIAATGITATACCATTAATGITCACTCGACACCCGGGGGGCAAAAAGAGAGAGAGAGAGAG		401 II-BSETTYFPhEASBABOYSThrValASBPOLYSGIUSGETIGLGELYSALGYALLYD HHEITHILLIHILIHIHIHIHIHIHIHIHIHIHIHIHIHIHIH	48i IlePhelisMetSerLeuLeuAlacysAlaLeuGluValValMetAlaThrTyrSerArg	56) GOUALAITPLEUSCRASPSCRPFOLCUPHCASPLCUITCHYSCINSCRIYSASPATGUU HILLIHIHIHIHIHIHIHIHIHIHIHIHIHIHIHIHIHI
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                                                                        621 ArqValAsnSerThrAlaAsnAlaGluThrGlnAlaThrSerAlaPheGlnThrClnLys 640
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Breast cancer related gene sequence SEG 1D NO:1210.
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stomach, lung; prostate; pancreas; carcinoma; antitumour; cancerous; "Tostatic; quo therapy; antineoplastic; Wilm's tumour; adenocarcinoma; Human: caucer: colon: breast; ovary: cesophagus; kidney; thyroid; dener ds

Homo sapiens.

14 DEC 2001

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2001WO 11510848 (O) MAY 2001; 20005

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20000S-235711P. 20000S-235720P. 20000S-23544 20000S 235840F. 20000S-235863F. 2356, 171 2356 3BP. 20000S -2000; 70007 20002 SEP SEP -138 SEF SEE SEP 200

20000S 236028F. 20000S 246034F. 20000S 246034F. 20000S 246109F. 20000S 246101F. 2000; 28 SEP 28-SEP SET SET SEP

-236891P. -237172P. 20000US - 246842P. 247174F. 237278F. 20000S - 20000S -2000015 2000; (0007 7000 2000; 2000 233 LX L.#0 70 SEP T. W. 70

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(AVAL.) AVALON PHARM.

Augustus M,

Young PE.

chemical agent to be fested for anti-neoplastic activity, and determining a change in expression of a gene of a signature gene set Seconding for anti neoplastic agent involves exposing cells to a WPI; 2002 188264/24. Suppert DR,

"laim 1; SEQ ID 1210; 44pp; English.

the present invention describes a method (MI) for screening for an

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181 TleSerThrGlulleAsuSerAlaLeuValLeuLysValSerTrpllethrPackenLeu

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618 CTCTTCAGCAAATEGGAAAGGACAFGTGAACTTATATATATTTGACACAAAAAGTTGG 627

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Horrigan S;

Carter KC, Ebner R, Endress G,

161 LeapheSerLysLouGluArqthrCysGlaLeatTelyrLouThrChnProSerSerSer

anti-neoplastic agent. The method involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, determining a change in expression of at least one gene (1) of a standard green set, where (1) comprises a sequence (S) selected from 6447 sequences (qiven in ABL51664 to ABL70110), or is at least 95% identical to (S), where a change in expression is indicative of anti-neoplastic activity. (1) has vivositaric activity and can be used for producing a product which is the data collected with respect to the anti-neoplastic agent as a structure and/or properties of the agent. MI can be used in the testil of cancer such as a structure and/or properties of the agent. MI can be used in the treatment of cancer such as colon, breast, stomach, lung, thyrotd, ocsophageal, ovarian, kidney, prostate or panereatic cancer, adenocarcibona, carcibona, elear cell cancer, intilitatina doublar cancer, aquambas cell carcibona, neutrendo rine carcibona, papillary carcibona and Wilm's tumour. 177 161 ILeCystiePhelleAiaAlaValAsploudlyAspMetSerPbethrPhethrGlubeu 120 121 GlutysAsnileGluffeSerValHistysPhePheAsnieutysGluffeAspThr 140 557 141 SerThrLysValAspAsnAlaMetSerArqLeuLysLysTyrAspValLeuPheAla 160 21 ProAlaProProProProProProGlaslaAspFrosluslnAspSerslyProGlu 40 61 CysginLysiculysfleProAspHisValArqGluArqAlaTrpLeuthrTrpCluEys 80 1 MetProProLysThrProArgLysThrAlaAlaThrAlaAlaAlaAlaAlaAlaAlaGluPro 20 41 AsplieuProLeuValArgileuGluPheGruGluThrCluGluProAspPheThrAlaLeu Sequence 4839 BP: 1534 A: 902 C: 880 G: 1523 T; 0 office; Connervative: Mismatches: Matches: indels: US:09 026 459A 51 (1 928) x ABL62873 (1:4839) 4787,00 49.84% 49.78% 44.77% Percent Similarity: Best Local Similarity: Aliqument Scores: Query Match: Pred. No.: Οy <u>a</u> 10 a a 9 â ō. q ŝ á ò ò ∂r ò 90

134	Cysvalleuasplyrbheiletysleuserproprometleutysclupromyrtys 240 		1878 (
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4 7	AlaarailealaLysGlnLemGluasmaspThrarqileIleGluValLemCysLysGlu 280 	Oy Db	621 / 1998 (
187	HISGLUSYSASBILGASDGLUVALLYSASBUVALTYFPHGLY 	QY QC	641 F
101	AsnsertenglytenValThrSerAsnglyteuProgluValGluAsnteuSe 	λ _O q _O	661 2 2118 c
121	TyrdludintleTyrLeuLysAsnLysAspLeuAspAlaArqLeuPheLeuAspHisAsp 340 	dq Db	681 7
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181 278	ThribednGinLeuMetMetMetTleLeuAsnSerAlaSerAspGinProSerGluAsnLeu 4	Oy.	741 A 1 2358 C
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46.1	LeutysSerGluGluGluArgteuSerHeGlnAsnPheSerLysLeuteuAsnAspAsn 4	0.7	821 T 1 2598 A
487	٠	du :	841 T 1 2658 A
77.	SerficserGloAsofouAspserGlyTbrAspLeussePheprofrpilefeussnval 52	O _Y Db	861 A 1 2718 A
5.21	tegrasulentiysalathteAsptheTyrtysValiteGluScrPheTtetysAlaGluCly (yo	881 G 1 2778 G
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661 ArgLeuAsnThrLeuCysGluArgLeuLeuSerGluHisProGluLeuGluHisIleIle
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UTHER PRODUCT OF THE PROPERTY 
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     21 ProAlaProProProProProProGluGluAspEroGluGluAspSerGlyProGlu 40
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                                                                                                                                                                                                                                                                    Recombinant; adenovirus: expression vector; TSG; small lung cancer; bystochretnoma; melanoma; retinoblastoma; sarcoma, pickle cell,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Ademoviral zector with deletion of viral protein IX contains foreign dence esp. encoding tumour suppressor protein for gene therapy of fumours, reduces contamination by wild type ademovirus
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Sequence 2995 BP; 975 A; 617 C; 594 G; 809 T; 0 other;
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AAU90059 standard; DNA; 2995 BP
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             141 SerThrLysValAspAsnAlaMetSerArqLeuLeuLystysTyrAspValLeuPheAla
                                                                                                                                                                                                                                                  161 LewPhaSertysicuSiuArqThrCysClutautieTyriaufhrCinProSerSerSer
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2539 GGAGGGAACATCTATATTTCACCCTGAAGACTCCATATAAAATTTCAGAAGGTCTGCCA 2598
                                                                                                                                                                                                                                                                                                                                                                   80] GlyGlyAsnilcTyrilcSerProlealysSerProfyrtysileSerGluGlyLoubro 820 [[[[[[[[[[]]]]]]]]]]]
                                                                921 ThrProThriysMetThrProArgSerArgileLauValSetileGlyGluSerPheGly 840
                                                                                                                                 841 ThrSerGluLysPheGlnLysIleAsnGlnMetValCysAsnSerAspArqValLeuLys 860
                                                                                                                                                                                                    851 ArgSerAlaGluClySerAsnProProLysProLeuLysLysLysLeuArgPheAsplicGlu 880
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                                                                                                                                                                                                                                                                                                                                  901 LeuAlaGluMetThrSerThrArgThrArgMctGlnLysGlnLysMctAsnAspSerMet 520
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Gene is taken from human chromosome 13q14 retinoblastoma (RB) cDNA. By installing a working CSS, cafe and specific treatment and prophylaxis can be given to cancer patients.
                                                                                                                                                                                                                                                                                      replacing ineffective cancer suppressing gene with cloned,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Cancer; cancer supressing gene; CSG; 13q14; retinoblastoma;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Location/Qualitiers
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                                                                                                                                                                                                                                                                                                                                                                                                    921 AspThrScrAsnlysGluGluLys 928
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   AAQ04713 standard; cDNA; 2994 BP.
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	çy	461	kellysSerGluGluGluArqLeuSerTloGluAsnPheSerLysLeuLasnAsnAspAsn	480
	qq	1519		15.71
	Οy	481	TepheHisMet Seri.cul.cuAlaCysAlaLonGluValWetMetAlathrigtSetArd	500
	qu	1579	ATTITICATATORE THAT I GOOGLOCOLOTTO I GARALON CACATATAGORA	26.43
	ζ	501	SerThrSerGlinAsnLeuAspSerGlyThrAspLeuSerPheFroTrp11eLeuAsnVal	520
	2	1639	AGTACATCTCAGAATCTTGATTCTGGAACAGATTGTCTTTCCCATGGATTCTGAGTGT	164
	0y	521	CuAsniculysAlaPheAspPteTyttysValifeCluSerPhettetysAladim3ly	540
	d G	1699	CTTAATTTAAAAGCCTTTGATTTTTACAAAGTGGTCGAAAGTTTTATCAAAGGAAAGGC	17.51
	0 O	541	ASTILOUTHTAEGOLUMOT LLOLYSHISLOUGLUAT GÖYSÖLÜH ISATA ELOMOT ÖLÜSÖT 	560
	ογ	561	LeuAlaTrpt.euSerAspSerProLeuPb-AspLeuTletysGluSertysAspArgilu	083
	q 0	1819	CTTGCATGGCTCTCAGATTCACCTTTATTTGATCTATTAAACAATCAAAGAA	187
	δŏ	581	GIYPTOThrAspHisteuGluSerAlaCysProLeuAsnLeuProLeuGluAsuAsnHis	6.00
	qq	1879	GGACCAACTGATCACCTGATCTGCTTGTCTTTTTTTTTT	194
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	qq	1949	ACTGCAGCAGATATGTATCTTTCTCCTGTAGATGTCCCAAAGAAAAAAGTTTCAACTAGG	661
	ς	621	ArgValAsnSerThrAlaAsnAlaGluThrGluAlaThrSerAlaPheGluThrGluBys	640
	20	1999	COTOTAAATTCTACTOCAAATOCAGAGATACAAGAAATCTCAGCCTTCTAGATTCTAGAAG	205
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Zhou Y;

Benedict WF, Hu S, Xu H,

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Buman retinoblasto	Heman retinoblasto	Human retinoblasto	Probe for retinobl	Modified retinobla	Modilied relinobla	Modified retinobla		Modified retinobla		Modified retinobla	DNA sequence of the	Retinoblastoma 94k	Modified retinobla	Modified tetinobla	cDNA of human reff	Refinoblasiona pro	Petinoblastoma gen	Wild type human re-	Bonen pll0-RB reti	Pertinoblastoma tum	Retinoblastoma tom	Refinoblastoma tum	Cancer supressing	Ferinoblastoma tum	erbNA encoding a re-	Human Rb110 cDNA.	Homan retinoblasto	DNA of human retin	Antiaense sequence	Direct tandem repe	Countract pMK10/As	Paratter PMKIL, AS	Construct pMK10/AS	Retinoblastoma pro	Retinationa pro
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Medified retinoblastoma famboar suppressor, blum protects, cancer therapy; consider proliferation inhibitor; ss.
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                                                                                                                                                                                                   protein (RTSP) of the invention. The proteins can be used for inhibiting excitator proliferation, when coadministered with a p53 pucies. The RTSPs can be used for treating discasses characterised by abnormal cellular proliferation, particularly caneers. The RTSPs have a broader spectrum of
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                                                                                                                                                                            This sequence encodes a modified relinablastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    100.0%; Score 3383; DB 19; Length 3383; 100.0%; Pred. No. 0;
                                                                Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                    Indels
                                                                                                                                                                                                                                                                                                                                    Sequence 3383 BP; 1104 A; 657 C; 623 G; 999 T; 0 other;
                                                                                        inhibiting cellular proliteration, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                               0;
                                                                                                                                                                                                                                                                                                                                                                                                                                  0; Mismatches
                                                                                                                              Maim 22; Page 218 222; 249pp; English.
                                                                                                                                                                                                                                                                                            artivity than wild type RISPs.
                                                                                                                                                                                                                                                                                                                                                                                                                               Matches 3383; Conservative
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Modified relinoblasiona tumour suppressor; KTSP protein; cancer therapy;
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                                                                                               3121 CICITORGAAAAAIGGAIATTALLAGAAALIAGAAAAAALLACIAALILLACACALLA (180
                                                                                                                                                              3181 GALTITATITIACIALIOGAAFOIGATALACIOTGIOTTGITITATAAAAFTITIOLILI 3240
                                                                                                                                                                                                         3241 TAATTAAATAAAAGCTGGAAGCAAAGTATAACCATATGATACTATCATACTACTGAAACA + 400
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                           3001 TGTTTTTATTAATTTALATGTALATTTTAATTTAACAGGGGCTGTAGAAATGT 3060
                                                                               3061 GTCCTATCTACCTTCCAAATGCAATTTGATTGACTGCCCATTCACCAAAATTATCCTGAA
                                          3301 GATTTCALACCICAGAAIGIAAAAGAACTIACIGAITALIFICTICALCAACTTATCTT
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Disclosure, Page 121–126, 249pp, English.
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cellular proliferation, when coadministered with a p53 proleip. The RISPs can be used for freating diseases characterised by abnormal cellular

preliteration, particularly cancers. The RTSPs have a broader spectrum of detivity than wild type RTSPs. (1) JAACCTO JGCACCCCCCCCCCCCCCCCCTCCTGAGGACCAGAGGAGACGACGGC 120 FILE CHIEFFELLE CONTROL OF THE CONTR 121 GGGGGGGGGCTGCCTCTCCTCCTCACCTTCACTTTGAAGAAGAAGAAGAACCTGATTTTACT 180 181 GOATTATGTCAGAAATTAAAGATACCAGATCAIGICAGAGAGAGAGAGGITAACTTGG 240 181 SCATIA1G1CAGAAATIAAAGAIACCAGAICATGICAGAGAGAGAGGIIGGIIAACTIGG 240 -51 TGGGGAATCTGTATCTTTATTGCAGTTGACCTAGATGAGATGTGATTTACT 360 421 GATACTAGTACCAAAGTTGATAATGTTGAAGACTGTTGAAGAAGTATGATGTATTG 480 421 GATAVORGTACCAAAGTIGATAATGOTATGTCAAGAGTGIIGAAGAAGTAIGGAGTAIIGAAIG 481 TITGGA TCTTCAGCAAATIGGAAAGGACATGIGAACTIAIAIAITTGACACCCAGC 540 HELLELLER HELLER 941 AGITGGATATCTACTGAAATAAATTCTGCATTGGTGCTAAAAGTTTCTTGGATCACATTT 600 541 AGTICSAIAICIACIGAAAIAAATICIGCATIGGIGCIAAAAGIIICIIGGAAICII 600 nul italtagetaaaggggaagtaftagaaafggaagatgatgtggtgatttgagtfa 660 **1 ATG*TATGTGTCCTTGACTATTTTATTAAACTCTCCCATGTTGCTCAAAGAACA 720 721 TATAAAACAGGTGTTATAQGCATTAATGGTTCACGTCGAACACCCAGGCGAGGTCAGAAC 780 81 ASSAST SCACGGATAGCAAAAACAACTAGAAAATGATAGAAAGTAGTAGTGT 840 731 -86178AAIICICIIKAAATITATAAAAIICIAAAAAICIICEAAAAAICIICI 789 461 GAGGIAGAGAAAAAQAIAGAAAIGAGIGCGAIAAAIIGITTAACITACIAAAAGAAAII 420 4. SAGGIA BGAAAAAGAIAGAAAICAGIGICCAIAAAIICIIIAAGIIACIAAAAAGAAAII 420 6) 1 TIATTASCTANAGGGGANGTATTACANATGGANGATGATCTGGTGATTCATTCAGTYA 660 841 AAASAACATGAATGTAATATAGATGAGGTGAAAAATGTTTGATTTCAAAAATTTTATACCT 900 1; Indels 171, Caps FORGITATION OF THE PROPERTY OF 94.5%; Score 3195.6; DB 19; Length 3555; Sequence 355% BP; 1171 A; 684 C; 653 G; 1047 T; 0 other; C; Mismatches Pred. No. 95.18; Chservative 7.11 TATAAAACAG-- -----Similarity Matcha 8 3379 CORP. Match : ---, t Š ž. 3 3 Š 5 3 5 ŝ $\frac{1}{2}$ Ξ 3 = 1 ÷ $\frac{2}{5}$

1081 AAAAGTAACCTTGATGAAGAGGTGAATGTAATTGGTGGAGACACAGTGAGTTAGGACTGTT 1140 1201 AATCTGATTTCCTATTTTAACAACTGCACAGTGAATCCAAAAGAAGTATACTGAAAAGA 1260 1090 GTGAAGGATATAGGATACATCTTTAAAGAGAAATTIGGTAAAGCTGTGGGACAGGCIGT 3149 1210 ICCATGCTIAAATCAGAAGAAGAACGATTATCCAIICAAAATTITAGGAAACITCIGAAT 1269 1330 AGCAGAAGTACATCTCAGAATCTTGATFCTGGAACAGATTGTCTTTTCCATGGATTCTTTTT 1489 1390 AATGTGCTTAAATTTAAAAGCCTTIGATTTTACAAAGIGAICGAAAGITTTAICAAAGCA 1443 1621 GAAGGCAACTTGACAAGAAAATGATAAAAGAITIAGAAAGGATGIGAACATGGAAICAIG 1600 1921 CAGAAGCCATTGAAATCTACCTCTCTTTCACTGTTTTATAAAAAGTG1A1CGGC1AGGC 1980 1810 TATCHCCCCCTAAATACACTTTGTGAACGCCTIC.GFCTGAGCACCCAGAATTAGAAAT 1849 1141 AIGAACACIATCCAACAATIAAFGAIGATTTTAAAIICAGCAAGIGAICAAACIICAGAA 1205 1261 GTGAAGGATATAGGATACATCTTTAAAGAAAATTTGCTAAAGCTGTGGGACACOGTTGT 1420 1150 GTCGAAATTGGATGACAGCGATACAAACTIGGAGIIGGCIIGTAIIAGGGAGIAAIGGAA 1209 1450 GAAGGGAACTTGAGAAGAGAAATGATAAAACATTTAGAAGGATGTGAACALOGAAGGAAGAA 1690 ACTACGCGTGTAAATTCTACTGCAAATGCAGACAAAAGCAACCTGAGTCTTCCAGACA 1749 1861 ACTRACGOSTIGNAATTIOTACTACAAATGCAGAGAAGGAACCAGAGCTIGGAGAAC 1920 901 TITALGAAIICICIIGGACIIGIAACAICIAAAGGAAGIICAAGAGGIIGAAAAICITICI 960 790 AAACGATACGAAGAATTTATCTTAAAATAAAGAIC AGATGCAAGAITALLLIGGAL 849 850 CATGATAAAACTCTTCAGACTGATTCTATAGACAGTTTTGAAACACAGAGAAAAAAA 910 AAAAGTAAGCTTGAIGAAGAGGIGAATGIAATFCCTCCACACTCCAGTTAGGACTGTT 970 ATGAACACTATCAACAATTAATGATTITTAAATTCAGGAAGTGALGAAGCITGAGAA 1570 GGAGAAGGACTAATGATGAATGGAALGIGGIGGIGGIGAIGIIGGIGGIGGAGAA 1750 CAGAAGCCAIIGAAAICIACICILIIGACIGIIIIAIAAAAAAGIGIAICGGCIAGCC 1381 TCCATGCTTAAATCAGAAGAAGGAFTATGCATTGAAAATTTTAGCAAACTTCTGAAL 1270 GACAAGATFTTGALAIGTGTTTATIGGGGTGGGGTGTTGAGGTTGTAALGGGALAIA ö ΟŻ q Š d q ò á qq á 3 q a qq 9 \circ ŏ ò ð Š

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      3010 TAATITATATGTATATTITITAATTTAACATGAACACGGGTTAGAAAATGTGTGTTATGT
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They can be used for the production of proteins such as tumour suppressor proteins which can be used for treating diseases characterised 401 10000AAFORTATOTTIALIGOAGCAGTTGACTAGATGAGATGTCGTTCACT 360 12. GGGGASSAGCIRGO GIGGICAGGO FIGAGOOTIGAAGAAAGAGAGAAGAAGTOTIGAGTI 180 121 AGGAGGANGTGOCTGTOGTGAGGTTGAGTTTGAGAAAAAAAAAAACGTGAFTFTACT 180 241 3AQAAAGTTTCATCTGTGAATGAAGTATTGGGAAGTTATATTCAAAAGAAAAAGGAACTG 300 401 TGGGGAATGTGTATGTTATTGGAGCAGTGACCTAGATGAGAGATGTCGTTCACTTTACT 360 **1 GABUTANDAAAAAAATAIAAAATOAGIGICCAIAAAIICITITAACIIACIAAAAGAAAIT 420 (4.) DAUGTACAGAAAACATAGAAATCAGTGTCCATAAATTTCTTTAACTTACTAAAAGAATTT 420 421 GAIACCAGIACCAAAGITGATAATGTGTTCAAGACIGIIGAAGAAGIAIGAIGIATIG 480 421 GATACCAGTACCAAGATGATAATGCTATGTCAAGACTGTTGAAGAAGTATGATGTATG 480 48 i TITOTATICITCAGGAAATIGGAAAGGACATGTGAACITATATATTGACACAACCCAGC 540 HER THEFT CONTROLLED FOR THE STANDARD AND THEFT FOR THE SACTOR AND 941 AGTTOGATATOTACTGAAATAAATTOTGGATTGGTGCTAAAAGTTTGTTGGATGACAITT 600 4; Indels 171; Gaps TACTATA CONTROL MANAGO CO CONTROL MANAGO CONTROL MANAGO CONTROL MANAGO CONTROL MANAGO CONTROL MANAGO CO CONTROL MANAGO CONTROL MA transactivation domain (TID) operatively attached to a tetracycline repressor protoin (IRP), the first sequence operatively positioned downstream of a promoter. The vector also contains a cloning site operatively prostlaned Marksteam of a basal promoter comprising a ferrorectively. The TREVS can be used to produce stable cell lines in which gene expression is tightly regulated by tetracycline. The present sequence appears in the specification, which describes tetracycline responsive expression vector (TREV), which contains a sequence encoding a fusion protein comprising a transcriptional 94.5%; Score 3195.6; DB 19; Length 3555; by abnormal cellular proliteration, particularly cancers. Sequence 3955 BP; 1171 A; 684 C; 653 G; 1047 T; 0 other; 0; Mismatches Distisure: Pages 145-150; 190pp: English. Pred. No. 0; 45.18; Most Local Similarity 95.1 Matches 3479; Conservative ā ä £ S ŝ Š = 5 ---3

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661 A DOCTATG FIGURE PERCHAPITA PRINA A CHECK CONTROCT PARA BARGA 720 661 AIGCIAFGIGICCTIGACIATITIATIAAACTCICCACCCCAIGTIGCTCAAAGAACCA 720 21 TATAAAACAGGTGTTATAGCCATTAATGGTTCAGCTGGAAGAGGCGAGGGGAGGTGAGAAG 780

7.21 TATAAAACAG------

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970 ALGAACACTATCCAACAALTAATGATGTTTTTAAATTCAGCAAGTGALGAAAGTTAAGAA 1029 1141 AEGAACACTATCCAACAATTAATGATTTTAAATEGGGAAGTGATCAACCTTGAGAA 1200 1090 GTGAAGGATATAGGATACATCTTTAAAGAGAAATTTGCTAAAGCTGTGGGACAGGTTGT 1149 1150 GECGAAAFFGGATCACAGGGATACAAACFFGGAGTFGGGTFGFATFAGGGAGTAALGGAA 1209 1321 GTCGAAAITGGATCACAGCGAIACAAACTIGGAGTTCGCTTGTATTACCGAGTAATGGAA 1380 1210 TCCATGCTTAAATCAGAAGAAGGATTATCCAT...CAAAATTTTTAGCAAAATTTCTGAAL 1269 1381 TCCATGCTTAAATCAGAAGAAGAAGATTATCCATTCAAAATTTTAGGAAATTTTGTGAAT 1440 1270 GACAACAITITICAIAIGICITIAIIGGCGIGGGGCGIIGAGGIIGIAAIGGCCALAIAI 1329 1330 AGCAGAAGTACATCTCGAGAATCTTGAATTCTGGAACAGATTTGTCTTTTCCCATGGATTCTG 1389 1501 AGCAGAAGTACATCTCAGAATCTTGATTCTGGAACAGAITTGTCTTTCCCATGGATTCTG 1560 1390 AATGEGETTAAAAAGGGTTTGATTTTTAGAAAGIGATGGAAAGTTIATGAAAGEA 1621 GAAGGCAACTITGAGAAAAGAAAATGATAAAAAGATTITAGAAGGATGTGAACATGGAATGATG 168U 1510 GAATCCCTFGCAFGCTCTCAGATTCACCTTTATTFGATTATTAATTAAGAAGGAG 1569 1630 AATONCACIGERAGAAAAIAIAITELICIETEIAAGAICIEGAAAAAAAAAGASII A 1689 1450 GAAGGCAACTTGACAAGAAATGATAAAACATTTAGAAGGATGTGAACATGGAATCATG 1509 910 AAAAGTAAACTIGATGAAGAAGGTGAALGIAALICCICCACACACICCAGIIAGGACIGII 969 781 AGGASTSCAUSGAIAGCAAAAQAACIAGAAAAIGAIACAAGAATIAITGAAGTICTGT 840 841 AAAGAACATGAATGTAATATAGATGAGGTGAAAAATGTTTALLTCAAAAATTTTATAGGT 950 731 ANTAMAIN NATIONARYTHAIARAINIANIGGACTICCAGAGGTIGAAAAICTITCI 789 790 AAACGATACGAAGAAATTTATCTTAAAAATAAAGATCTAGATGCAAGAFTALLIFIGGAL 849 850 CATGATAAAACTCTTCAGACTGATICTATAGACAGTLIIGAAACACAGAGAAAAAAGA 909 1570 GGGGAAGGAACHGATCACCTTGAATCHGCTTIGTCTTAATCTTGCG CLOCAGAA 1261 GTGAAGGATATAGGATACATOTTTAAAGAGAAATTTGOTTAAAGGTGTGGGGAGGGTTG 731 a G ò 3 퍒 qq ò qq qq ô 윤 ò ŝ ò g 6 qq qq ò

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ANTANAGESTAAATTOTANTGCAAATGAAGAAAAAAAAAAAAAAAAAAAAAAAAAA	FYSGASICCALIGAATCIACTICICLIFCACTOTTTTATAAAAAGIGIALCGGCTAGCC 	HATCHCOCHAALACACHTGGACCCHCTCCCCCACACACACACACACTTACAACACTTACAACACTTTTTT	0 AFCATCTGRACCTTTTCCAGCACACACGGAATGAGTATGAACTCTGAGAGAGA) PALLEGIA-CAAA HARGARGERE POPATORA POPATA POPAAAO HARAAA HARAGO HELLEGIA HELLEGIA HARGAAA HARAGO PALLEGIA HELLEGIA POPAAAO HARAGAAAA BARAAAA BARAAAAA BARAAAAAAAAAAA) PH AAATTCAAAATCATGTAACAAGGATCTTGCTCATGCTGTTGGGGGGCAATTTTTTTT) TPPAAACGTGTTTTGAFCAAAGAAGAGGTGTATGATTCTATTATAGTATCTGTGTATAAACTCG - - - - - - - - - - - -	0 GETTECATOCAGACACTICAAAACAAATATETGCAGTATGCTTGCACCAGGCCCCTACC 	0. 1010 A WAATAM TOT AND TOT TO CAADOM TATAM TOTAM TOT	ATTOCTOGRESSAN'ATCTATATITEANCOCTGAAGAGTCCATATAAAATTTCAGAAGGT	FTGPPAACACCAACAAAAA GACLCCAAGA CAAGAACTTACTTACTTACATTGGTGAATGA 	O TEMBORALTE IGAGAACI FEGARAAA AAATEGATOO ATGAAGAAGAACAGOO TOO COOLO TELLET TEL	0 TTTAAANGAAGTGETGAAGGAAGAAGCTGGTAAACAGTGAAAAAACTAGGTTGAT 	U ATTGAMGGATCAGA GAMOCAGA GGAMOTAMACATCTCCCAGGAGGCGAAATTTCAG HITTITTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	J. PADAAACHGGAGAAA BAATHCHACTGGAAGGGAATGGAAAAGAAAATGAATGAT TELLTITTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT) ABYATSBATAVOTEVAAN AAGAANAGABAGEEGGACHEEGGGACACTGT 	DEGLACAPTETGRADICATOR CHEACARA IGHANIA HARACTTICCEAGGITETGT FELCET FELC	UTTATOBORANTHALIATORICAGERTOLIA GARANALGI GEAGA IGCAATTE THEFTELLE HELLELLE HELLELLE HELLELLE HELLELLE HELLELLE HELLELLE HELLELLE HELLE HELLE HELLE HELLE HELLE GEAGATA AAA AAAA GAGAAA IGCAAATTE HELLE GEAGATA AAAA AAAA GAGAAA IGCAAATTE HELLE GAGAATTAAAA AAAAA GAAAAA GAAAAA GAAAA GAAAA GAAAA GAAAA GAAAA GAAAA GAAAA GAAAA GAAAA GAAAAA GAAAAA GAAAAA GAAAAA GAAAAA GAAAAA GAAAAA GAAAAAA	0 GITTGGGTGATICCTAAGGCACITGAAAIGITAGICAIIGITATTTATACAAGATIGAAA
1690	1750 1921	1830	1870	1940	1990	2050	2110	2170	22.80	2290	2521	2410	2471	25.40	2540	282]	2710	2770
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hEST2; telomerase; catalytic subunit; reverse transcriptase; lile-span;
retinoblastoma; p53; tumour suppressor; inhibitor; arteriosclerosis;
proliferation; immortal; tumour therapy; macular degeneration; activator;
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                                                                                               3001 ATCTTGTGTAAATCCTGCCATTTAAAAAGTTGTAGCAGATTGTTGCTCTTGCTAAAGTAA
                                                                                                                                                                                                                                 2890 AATTGCTGTGTTTATGGAIAMTAGAAALGGGGGGTGGGGAGGG GAIAAGG
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Hannon GJ, Beach DH;

WP:: 2000-400055/34.

New method for increasing the prollierative capacity of cell lines comprises the bilarceins aperts recognify activities (electric activity and reversibly inactivating RD/INK4 and/or p53 pathways useful in treating age related discases

Lain 5; Page 121-123; 123pp; English.

The invention concerns methods and readents for extending the life span, activation of mitotic divisions, of a cell. The method relies on artivation of an telemenase activity and inhibition of once to both of a retination of the life span division cycle. Building of INK4 and cdk6, releases the cells into the division cycle. Binding of INK4 tamily members, e.g. the tumour suppressor picknear, inhibits binase activity and results in growth arrest. Refunctivators can selectively and results in growth arrest. Refunctivators can selectively and recessibly inactivate an superiors. Refunctivators can selectively and recessibly inactivate and strost. Refunctivators can selectively and recessibly inactivate and strost. Refunctivators can selectively and recessibly inactivate and safe on a sead in the methods other molecules which can suppressor also also be used in the methods other molecules which also be used in the methods of the molecules which there it may not or more or residues K22, R24, H95 and/or D97. With all oncomponent why also be used. The methods are useful for the Rb and picinked applicative capacity of cells. The cells are increasing the profilerative capacity of cells. The cells are subsequently of use in pharmaceutical and commette preparations and arterosclerosis. The cells can also be used to replace tumour cell increasing and differentiation. Long lived (immortal) cells could also be belonesed in the products.

Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other;

25× 083A83ACCTGCCTCTCATCAGGCTTGAGTTTGAAGAAACAGANAAACTGATTTAATG 312 82 CATTAIGICHABAATTAAAGATTACCAGATGTTGTGAGAGAGGTGGTTTAAGTTGGG 241 413 CALLARGICAGAAATTAAAGATAAGATGATGAGAGAGAGGGTTGGGTTTAAGTTGGG 372 102 GGGGALCIGIAICTIIAITGCAGCAGTTGACCAGTAGATGTGTGTTCACTTTAGTG 361 493 ACCTACAGAAAAACATAGAAATCACTGTCCATAAATTTCTTTTAACTTACTAAAAGAAATTG 552 4; Indels 171; Gaps 94.4%; Score 3194.6; DB 21; Length 4839; 95.1%; Pred. No. 0; 0; Mismatches Conservative ocal Similarity Matches 3478; 5

1391 AFGEGGTFAATFTAAAAGGGTTTGATFTTTACAAAGTGAAGGTHTTALCAAAGCAG 1450

1033 TTATGAATTGTGTTGTAGTTGTAAGATGTAATGCAGTTGCAGAGGTTGAAATGTTGTA 1092 971 IGAACACTAICCAACAATIAAIGAIGATIIIAAATICAGCAAGIGAIGAACTICAGAAA 1030 1031 APCEGAPPECCTATETTAACAACEGCACAGEGAAFGCCAAAAGAAAGTAFACEGAAAAGAG 1099 1091 TGAAGGATATAGGATACATCTTTAAAGAGAAATTTGCTAAAGCTGTGGGACAGGGTTGTG 1150 1151 TCGAAATTGGATCACAGGGATACAAAGTTGGAGTTCGCCTGTATTACCGAGTAATGCAAT 1210 1211 CCATGCTTAAATCAGAAGAAGAAGATTATCCATTCAAAATTTTAGGAAAGTTCTAAATG 1270 1633 GCAGAAGTACATCTCAGAATCTTGATTCTGGAACAGATTTGTCTTGCCGATGGATTCTGA 1692 973 AAGAACAIGAAIGIAAIATAAGAIGAGGIGAAAAAIGIIIAIIIICAAAAAIIIIAIAAAAL 1331 GCAGAAGTACALCICAGAATCITGATICIGGAACAGAITIGICITICCCAIGGAIICIGA 1390 1513 CCATGCTTAAAICAGAAGAAGAAGATIAICCATICAAAATITTAGCAAACIICIGAAIG 1572 482 TTGCACTCTTCAGCAAATTGGAAAGGACATGTGAAGTTATATTTGACAAAAGCAAGT 941 913 GGAGTOCACGGATAGCAAAACAACIASAAAATGAIACAASAAITAIIGAAGIIGTOIGIA 972 791 AAGGAIAGGAAGAAGTTAFCTTAAAAAIAAAGAICTAGAIGCAAGATAITITIGGAIC 850 851 ATGATAAAACTCTTCAGACTGATTCTATAGACAGTTTTGAAACACAGAGAACAACAAGAA 910 793 IGCIAIGIGCCIIGACIAIIIIAIIAAACICICAACICCCAIGIIGCICAAAGAACAI 731 GGTCGAATTCTCTTGGACTTGTAACATGIAAISGACTTGCAGAGGTTGAAAAICTTTCTA 1271 ACAACATITITCATATGICITIATIGCGIGGGGIGTIGAGGIIGIAATGGGCGACATATA 673 GELEGALARMAAMMAAAMMOGALMOGEGEAAAAGETEGELGOALGAGALEE 1453 TCGAAATTGGATCACACATACAAACITGGAGIICGGIIGTAIIACCGAGTAATGGAAT 722 ATAAAACAG-----731 ----qq ે £ a ò 3 Ś g

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                                          2531 AGAAACTGGCAGAAATGACTTCTACTCGAACACGAAATGATAAAAAG AGAAAALGAATGATA 2530
                                                                                                                                                   2651 TACACCICIGGAIICAIIGICLCICACAGAIGIGACIGIAIAACIIIC CAGGIICTGII 2710
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              The present sequence encodes a human androgen receptor coactivator designanted Rb. Androgen receptor to activator proteins from the present invention can be used in serventing assays to identify andidate pharmaceutical molecules for the ability to promote or inhibit the interaction of androgen receptors and androgen responsive cionents to modicate and androgen responsive cionents to modicate and coactivity. The identification and characterisation and androgen receptor co-activators such as those of the invention will
                                                                                                                                                                                                                                                                                                                                                                                                                                   Novel androwen receptor-associated proteins used to detect androgenic or antiaudrogenic activity in screening assays for candidate pharmaceutical molecules which promote or inhibit the activity -
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        122 CGGARGTAPPTGGTPTGGTPAGGTTGAGTTTGAAGAACAAGAAGCTGATTTAGTG 181
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Human: androqen receptor coartivator: ARA51; ARA55; ARA24; detection;
Rt: androgenic; antiandrogenic; identification; prostate cancer; ss.
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                                                                                                                                            /note- "androgen receptor coactivator"
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2951 CTGTCTGACTACTTTGCCTTCTTTG1A0/A1AIAGGIGATGTTTGTTGTTTTATT
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stomach, lunc, prostate, paneteas, carcinoma, antitumour, cancerous,
yr static, acce therapy, antineoplastic, Wilm's tumour, adenorare/boma;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Endress G. Horrigan S.
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                                                                                                                                                                                                                                                                                                                                                                          Breast camber related gene bequence SEQ ID MO.1210.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Ebner R.
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APD-2879 Standard: DNA: 4839 BP
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2000US 234509P.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   2000US-234009P.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             236032P.
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oesophaqeal, ovarian, kidney, prostate or pancreatic cancer, adenocarcinoma, carcinoma, clear cell cancer, infiltrating ductal cancer, infiltrating lobular cancer, squamous cell carcinoma, neuroendocrine
                      anti-neoplastic agent. The method involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, determining a change in expression of at least one gene (I) of a signature gene set, where (I) countries a sequence (S) solected from 8447 sequences (given in AHEFEGA to AHIZOIIO), or is at least 95% identical to (S), where a change in activity of is at least 95% identical to (S), where a change in activity and can be used for producing a product which an anti-neoplastic agent, and can be used for producing a product which is the data collected with respect to the anti-neoplastic agent as a structure and/or properties of the agent. MI can be used in the structure and/or properties of the agent. MI can be used in the treatment of cancer such as colon, breast, stomach, lung, thyroid,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          182 CATTATGLCAGAAATTAAAGATACCAGATCATCLCAGAGAGAGAGCLLGGLLAACLLGGG 241
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              373 AGAAAGTTTGATGTGTGGATGGAGTATTGGGAGGTTATATGTGAAAAAGAAAAAGGAAGTGT 432
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  482 IIGCACICIICAGCAAAIIGGAAAGGACAIGIGAACIIATATATATTIGACACAAGCA 541
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        602 PATTAGCTAAAGGGGAAGTATTACAAATGGAAGATGATCTGGTGATFTCATTTGAGTTAA 661
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                122 TANGARY GOLF TOTO A BETT SASTITS AND A SASTAT SANDRANCE 181
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        422 ATACCACTACCAAGTIIGATAATGCTAIGIGAAGACTIGTIIGAAGAAGTAIGAATGI 481
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    4; indels 171; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        The present invention describes a method (M1) for screening for an
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            302 ACCORANT TENTATION TO ANY ACTIONAL TABANCA CONTROLL AND ALCOHOMOSTICAL SACTIONAL PROPERTY.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          94.49; Score 3194.6; DB 24; Lenath 4839;
95.18; Pred. No. 0;
Uive 0; Mismatches 4; indets 171; C
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   carcinoma, papillary carcinoma and Wilm's tumour,
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ı,	1:14	TIABBARTETETETEGACTESTAACAFCTAATGGACTTCCAGAGGTTGAAAATCTTGTA	1092
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ے	1 45 5	TGAAGGATATAGGATACATCTTTAAAGAGAAATTTGCTAAAGCTGTGGGACAGGGTTGTT	452
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οy	1751	751 AGAAGCCAITGAAATCTACTCTTTCATGITTTATAAAAAGTGTATGGGAAGGGTAGTTTTT
qq	2053	AGAAGCATTGAAATCTACTCTCTTTCACTGTTTTALAAAAAGTGLAFAGGTLAGACT
οy	1811	ATCLCCGGCDAAATACACTTGTCAACGCCTTOTGTCTCACACCACACATA
q	2113	ATCLCCGCTAAATACACTTGTGAACGCCTTGTGTGTGTGTGTGT
ολ	1871	TCATCTGGACCTTTCCAGCACACACTGTAGAATGAGTATGAATTGAGAATAGAATAAGACTATTCATAGAATAAGACACAAATGAAATAAGAATAAGAATAAGAAATAAGAAATAAGAAATAAGAATAAGAAATAAGAAAAAA
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ΟY	1931	ATTTGGACGAAATTATGATGTGTTCCALGTATGGCALATGCAAAGTGAAGAATATAGAC
ୟୁପ	2243	ATTIGGACCAAAITATGATGTGCTCCATGTATGCAAAGTGAAGAAIATAGACC
ογ	1881	FTAAATTCAAAATCATTGTAACAGCATACAAGGATCTTCCTCATGCTGTTCAGGGGGACACT
Db	2293	TTAAATTCAAAATCATTGTAACAGCATACAAGGAGATCTTCATCATGTTTTTTTT
δò	2051	TCAAACGTGTTTTGATCAAAGAAGGAGTATGATTCTATTATATTCTATAAVTCGG
1010	2353	TCAAACGIGTTTGATCAAAGAAGAGAATAATAATAATAATAATAATAA
OY	2111	TCTTCATCCACACACACAAATATTTTGCAGIAIGCTTCCACCAGGCCCCIACC
qq	2413	TCTTCATGCAGAGAGAGAAAAAAAAAAAAAAAAAAAAAA
Oy	2171	TGTCACCAATACCTCACA TCCTCGAAGCCTTACAAGTTCCTAGTAGTACTCTTACCAATACCTACAAGTACAACAAAAAAAA
90	2473	TGTCACCAATACCTCACATTCCTCCAAGCCCTTACAAGTTTCCTGATTCACTTACAAGT
ć	2231	TTCCTGGAGGGAACALCTATATACCCCCGAACACTCCATATAAAATTTCAGAACGTC
Db	2533	TECTGGAGGAACATCTATATTTCACCEGGAGAGTCCATATAAAATTTAAGAAGTC
ÓΥ	2291	IGCCAACACAACAAAATGACTCCAAGATCAAGAATCTTAGTAAATTGATGATTGAT
Ob	2593	TGCCAACACAACAAAAATGACTCCAAGATCAAGAATCTTAGTATTGGTGAATCAT
οy	2351	TCGCGACTITCTGAGAAGTTCCAGAAAATAAATCAGTATGTATGAACAAAAAAAA
qu	2653	PGGGGACTICTGAGAAGTICCAGAAAATAAATGAGATGATGTATGTAAGAGAGAGTGTATGT
çò	2411	TCAAAAGAAGTGCTGAAGGAAGGAACCCTGTAAACCAGTGAAAAAA TAGGGTTTGATA
qc	2713	TCAAAAGAAGTGCTGAAGGAAGGAAGTCTGATTGAATTGAAAAAATATTTTTTTT
ςŏ	2471	TIGAAGGAICAGATGAAGAAGGAATIAAAAAITAAAGAAGAGAGAGTAAAAATTAAGG
QQ	2773	TTGARGGATGAGAGAGAGAGAGAAATAAAAAAAAAAAAA
οy	2531	AGAAACTGGCAGAAATGACTT CTACTTCGAACTACGAATACAAAAAAAAAA
qu	2833	AGAAACTIGGCAGAAATGACTTGTACTGGAACAGGAATGCAAAAGCAGAAATGAATG
Óy	2591	GCATGGATACCTCAAACAAGAGAAATGAGGATCTCAGGACCTTGGTGGACACTGG
qí	2894	GCATGGATACPTCAAACAAGGAAGAAATGAGGATPTFCAGGACFTTGTGTAGTACTGTG
ΟŸ	2651	TACACCT CTGCATTCATTGTCTCTCACACATGTCATAACTTTTCCTACGTTCTGTTTTTCTTTTTTTT
qq	2953	TACACCTCTGGATTCATTGTCTCACAGATGTGACTGTATAACTTTCCCAGGTTCTTTT

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M 400 belocked as one takes suppressed. RISP prototor cannot than approved tale proliferation inhibitor; ss.
                     2711 IATGGGGAJAITIAAFATGTGGAGCTGTTTTGTGGGATAIAAAATGTGGAGATGGAAFTG 2770
                                                                                2771 ITTGGGTGATTGCTAAGGCANTTGAAATGTTAGTGATGTTATTATAAGAGATTGAAAA 2830
                                                                                                      28.3] INTERPRIMENTAND PROPERTY TANDANG PROPERTY CONTROLL OF A SAGE AND A SAGE
                                                                                                                                                                                     2891 ATTGCTGTGTTTTATGGATAGTAAGAATGGCCCTAGAGTGGGGGTCCTGATAACCCAGGC 2950
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      331) PICAGAATGTAAAAGAACITACIGATTATTTTGTTCATCCAACTTATGTTTTAAATGAG 3370
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       3253 CIGICIGACHACHTGCCTTCTTTGACATAAAGATGATTTGCTTTGTTTTTATTTTATTTTATA
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                                                                                                                                                                                                                                                                                                                                                      Meditied retinoblastoma tumour suppressor gene.
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X 2 X X
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process (MISE) of the invention. The process can be used for inhibiting can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  11 CCGGAGGACCMCCTCAGGCTTCAGGCTTTGAAGAACAGAAGAACCTGATTTTACT 180
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    241 GAGAAAGPPPGARGTGFGGATGGAGTATFGGGAGGTTATFICAAAAAGAAAAAAAAGAAACFG 300
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          241 GAGAAAGTITCAICTGIGGATGGAGIAITBGGAGGITAITCAAAAGAAAAAGGAAACIG 509
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     A61 GAGTIACAGAAAAAATIASAAALCAGIGICCAIAAAIICIIIAACIIACTAAAAGAAATT 420
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      421 GATACCAGFACCAAAGTIGATAATGCTATGTCGAAGA/TGTTGAAGAAGTATGATGTATG 480
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             481 TITGCACTCTTCAGGAAATTGGAAAGGACATGTGAACTTALATATTTGACAAAAACACAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             481 TTTGCACTCTTCAGCAAATTGGAAAGGACAFGTGAAGCTTATATTTTGACACACACAGC 540
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     This sequence encodes a modified retinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for Labi
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                                                                                                                                                                                                                                                                                                                                                                                                                                                 Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Sequence 3554 BP; 1170 A; 683 C; 653 G; 1048 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        inhibiting cellular proliferation, particularly cancer
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0; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           71aim 22: Page 226-238; 249pp; English.
                                                                                                                                                                                                                                                             Benedict WF, Hu S, Xu H, Zhou Y;
                                                                                                                                                (BAYU ) BAYLOR COLLEGE MEDICINE.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Best Local Similarity 95.0%;
Matches 3377; Conservative
98WO-US03041
                                                                          97US-0038118
                                                                                                                                                                           UNIV TEXAS SYSTEM
                                                                                                                                                                                                                                                                                                                                    WP1: 1999-480709.41.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Local Similarity
                                                                                                                                                                                                                                                                                                                                                                       P-PSDB; AAW69376.
19-FEB-1998;
                                                                          20-FEB-1997;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Query Match
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<u>Q</u>
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Ę	7н1	AGGAGGGACACGATAGAAAACAACTAGAAAATGATAGAAGAATTATTGAAGTGTGT	840
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5 £	1510	GAALCCTIONALGCTCTCAGAICACCHIALIGATCTATAAACAACAACAC HILLELLIGHELLIGHELELELIGHELLIGHELLIGHELLIGHELLIGHELLIGHEL GAACCCTGATGCTCAGCTCTCAGAITVACCITTATTGATCTTAITAAAGAACAACGAAGGAC	1569 17 4 0

Qy Dt	1570 CGAGAAGGACCAACTGATC 	ACCHGAAFCTGCTGCTGTAACTGGTGTGTGTGTTTTTTTTTTTT	6.791
ΟΥ Db	1630 AATCACACTGCAGCAGATA 	IGTATCTTCTCTCTAASALCTCCAAASAAAAAGSTTCA 	1689 1860
ç S	1690 ACTACGCGTGTAAALTTE 	CLOCAAA LOTAGAGATAYAADTAATTIFYADOOLI LOTAGATTI ELITTII TITTII TIT	1749
δο da	1750 CAGAAGCCATTGAAATCTA 	CONTOCTITION OF THE PROPERTY O	1809
Oy Dp		FTTGFQAACGCCTCTGTGTCTGAGTACCTAGAATAGAACAT FFLFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	1869
oy ob	1 2	AGCACACCOCOCACAAOCACAACAACAACAACAACAACAACA	6761
yo da	1930 CATTIGGACCAAATTATGA	TGTGTTCCALGTATGGCATATGCAAGTGAAGAATATAGAC 	1989
Oy Db	1990 CTTAAATTCAAAATCALLC 1111111111111111111111111111111111	TAACAGCATAGAAGAATCTTCCTCATGCTGTTCTTCTAGAGAAAA 	6407
Qy Db	2 2	AAGAAGAGAGATATGATTCTATTATTATTATTATTATTATTATTATTATATTATATTATTATA	2109
Oy DD	2 3	AAACAAATATTTTGCASTATGCTTCCACCAGGCCCCCTACCCAAGCACAAGTTTTTTTT	2169
çy G	01 01	TECTCGAACCCTTACAAD FECTAGLE ACCCTTACA TITLITITITITITITITITITITITITITITITITITI	2229
OY Db	2 2	ATATTTCACOCCGAAGAGOOTATATAAAATTTOAGAAGT. TITTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	2289
Oy Dp	2 2	TGACTCCAAGATCAAGAATCTTAGTATCAATTGGGAATCA . FILLELLELLELLELLELLELLELLELLELLELLELLE GACTCCAAGALCAAGAATCTTAGTATCAATTGGATCA .	2349
ςο da	8 8	FORGAAAATAAATOAGATONTATGIAAOAOAGAAOATOTTOTTOTTOTTOTTOTTOTTOTTOTTOTTOTTOT	2409
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ò à	2 2	470 ATTGAAGGATCAGATGAGGAGGTGAACTAACATCCCAGGAGAGTCAGG 252 	2529
Gb	8 8	CTICTACTOGAACACQAATSCAAAAQCAGAAAATGAATTETTITTITTITTITTETTE CTTCTACTOGAACACGAATGCAAAAGCAGAAAATGAATGAT	2760
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λο :	.7	GICTCICACAGAIGIGACIGIAIAACIIICCCAGGIICICI	2709

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Modified reliabliasions based suppressor, RISF protein; cancer therapy; cellular proliferation inhibitor; ss.
                                                                                                                                                                                                   268: HATGARAMAN GILLARIA HATA HATA HATA HATA HATA HATA HATA ARATTA 2940
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       282] GIACACCICIGGATTCATTGTCTCTCACAGA1GFGACIGTATAACIFFCCCAGGTFCIGF 2880
                                                                                                                                      2.1 - TIATGEREAMMATTTAATATCTTCAGCTCTTTTTGTGGGATATAAAATGTGCAGATGCAATT 2769
                                                                                                                                                                                                                                                                                                                                         2829
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       *: ** AAAAA: SZATATTAFIAGAAATTAGAAAAATTACTAATTTTAGACATTAGATTTAFT 3189
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               ***! AAAAAFSJAIATIAITAGAAATTAGAAAAAATTACTAATITTACACATTAGATITTAIT 3360
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 (190) TIACIALIOGAATCPGAFAFACTGTGTGTGTTCTTTTTAAATTTTGCPPTFAAAT 3249
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              (**) :TATTATTGGAATCTGATATACTGTGTGTGTTTTATAAAATTTTGCTTTTAAATTTAAAT 3420
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                (2.5.) NANAGUTGGANGCAAGTATAACCATATGATACTATCATACTACTGAAACAGATTTCATA 3309
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             442) AAAAGGIGGAAGCAAAGIATAACGATATGATACTATCATACTGCTGAAAGAGATTTCATA 3480
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Modified retinoblastoma tumout supplessor gene.
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protein (RTSP) of the invention. The proteins can be used for inhibiting calbuar proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      361 GAGCIACAGAAAAACAIAGAAAICAGIGICCAIAAAIICIIITAACITACTAAAAAGAAAIT 420
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        121 CCGGAGGACTGCCTCTCGTCAGGCTTGAGTTTGAAGAAGAAGAAGGGAGTTTTAGT 180
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          301 TGGGGAATCTGTATCTTTATTGCAGCAGTTGACCTAJATGAGATGTCGTTCACTTTTACT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     this sequence encodes a modified retimoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           93.7%; Score 3169; DB 19; Length 4377;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Sequence 3377 BP; 1113 A; 654 C; 626 G; 984 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      inhibiting cellular proliferation, purthousart, cuncer
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Claim 22; Page 210 215; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                         Hu S, Xu H, Zhou Y;
                                                                                                                                                                                                                                                 (BAYU ) BAYLOR COLLEGE MEDICINE
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           activity than wild type RTSPs.
                                                                                 98WO-1190 104 ].
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                                                                                                                                                                                                                                                                                       ( FEXA ) UNIV TEXAS SYSTEM
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                                                                             19-FFR-1998.
                                                                                                                                                               20-FEB-1997;
27 - AUC - 1998
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assays immune complex; ss.
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A method for detecting the presence, in a tumour sample, of a protein the absence of which is associated with a neoplasm, comprises producing an autilody to the protein and then contacting the arithedy with the tumour sample, manne complexes indicate the presence of the protein in the sample. The method may be used in the detection and treatment of a defective human gene related to
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        244 AAAGTTTCATCTGTGGATGGAGTATTGGGAGGTTATATTGAAAAGAAAAAGGAACTGTGG 303
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                304 GGAATCHGMATCMTTGCAGCAGTHGACCTAGATGAGATGTCGTTCACTTTACTGAG 353
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       184 ITATGTCAGAAATTAAAGAIACCAGAIGAIGICAGAGAGAGAGAGTIGGTTAACTTGGGAG 243
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     364 CIACAGAAAACAIAGAAATGAGIGIGCATAAAIIGIITAACTAAAAAGAAATIGAT 423
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        418 ACCASTACUAAAGIIGAFAA BOTAFG DOAAGATGTTGAAGAAGTATGATGTATTGTTT 477
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   478 GCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATTTGACAGAAGCCAGCAGT 537
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     664 CTATGTGTGTGTGTTGACTATTTTATTAAACTGTCACCATGTTGCTCAAAGAAGCATAT 723
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          658 CYATCHCCTHCACTAITHTAITAAACHCTCACCAIGHIGHIGHCAAAAGAACCAIAL 717
                                                                                                                                                                                                                                                                                                                                                                                                                                     indels 174; daps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                          484 GCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTTATATTTGGCACAACCCAGCAG
                                                                      Diagnosing the presence of defective retinoblastoma alleles -
comprises compuring genetic material corresponding to a normal
human retinoblastoma with DNA from a patient.
                                                                                                                                                                                                                                                                                                                                                                                               OB 15; Length 4597;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 4597 BP; 1489 A; 841 C; 812 G; 1455 T; 0 other;
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                                                                                                                                                                                                                                                                                                                                                                                                                  Pred. No. 0;
); Mismatches
                                                                                                                                                                                                                                                                                                                                                                                               93.68; Score 3165;
                                                                                                                                                      Example 2(2); Figure 7: 18pp: English.
                                                                                                                                                                                                                                                                                                                cancer, in particular retinoblastoma.
                                                                                                                                                                                                                                                                                                                                                                                                                Best Local Similarity 95.0%;
Matches 3372; Conservative
              WEI, 1994 272746,734.
P-PSDB; AAK58568.
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27.1. 106616A116C1AAGCCACTTGAAATGTFACTGTTATTTATACAAGATTGAAAATG 2832
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244 AAAGTTTCATGTGGGATGGAGTATTGGGAGGTTATATTCAAAAGAAAAAGAACTGTGG +03
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        124 GAGGACCTGCCTCTCGTCGTCAGGCTTGAGTTTTGAAGAACAGAAGCTGATTTTACTGCA 183
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    119 GA-GACCTGCCTCTCGTCAGGTTGAGTTTGAAGAAAGAAGAAGAAGATTTTACTGGA 177
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Isolated human retinoblastoma gene - used to develop products tor
analysing predisposition to retinoblastoma and for the detection and
Arealment of retinoblastoma
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Indels 174; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             The
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      retinables one age to Absence or mutalion of the Rt acre (see also AAX04502) predisposes an individual to retinables from a Tochsolate Ab converse an individual to retinables from a human chromosome 13 lambda phage library, was used in a chromosome walk to isolate and map 30 kb of gonomic DNA surrounding the H3-8 sequence. Fraqment p7H30.TX (ATC 97500) was obtained, and was used as a privale of screen a cNNA library that had been constructed from an adenovirus 12-transformed human embryonic retinal cell
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          gene can also be used to synthesize Rb polypeptide (see AANO1542) f
use in the treatment of individuals determined to have a defective
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 gene, CDNA or a fragment of the gene such as one of the 27 excus
or 26 introns, can be used in a claimed method for detecting a
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        linc. This provided cloud p4.7R (ATCC 97383), which in Marthern blons aross-reacted with a 4.7 Re transcript in transformed rethnal cells which was not present in 4 retinoblastoms and one osteosarcoma cell samples. Rb nucleic acids comprising the Rb
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           This is the nucleic acid sequence of a cDNA of the normal human
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Match 133.6%; Score 3165; DH 20; Length 4597; Local Similarity 95.0%; Pred. No. 0; Local Similarity 95.0%; Pred. No. 0; Local Similarity 95.0%; Pred. No. 0; Mismatches 5; Indels 1741;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            deletion or point mutation in the Rb gene of a human patient.
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                                                                                                                                                                                                                                 (MASS-) MASSACHUSETTS EYE & EAR INFIRMARY.
                                                                                                                                                                                                                                                                                                                                                  Dryja TP, Friend S, Yandell DW;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Claim 8; Fig 5; 32pp; English.
86US-0895163.
88US-0146525.
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                                                                                                                                                                                                                                                                                                                                                                                                                           WPI; 1999-094898/08.
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    11-AUG-1986;
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AANW1369 standard, DNA, 4597 BP.

RESULT TI AANBIA69 AANE 1365.

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using genetic material corresp. to a normal
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            64 CONCEGERACIONOGO CONTROLISMOS ASSESSORAS CARACTARISMOS 123
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 178 TIAIGTCAGAAATTAAAGATACCAGATCATGTCAGAGAGAGGTGGTTAGTTTGGGAG 247
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        6; Indels 174; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         <u>184 FTATCFCAGAAATTAAAGATACCAGATCATGAGAGAGAGAGGTTGGGTTAGGGGGTTGGGAG</u>
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      244 AAAGTIICAFCIGTGGAIGGAGIAITGGGAGGIIAIAIICAAAAGAAAAAGGAAAHGH
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   human retinoblastoma gene or a unique sub-region
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                                                                                    Retinoblastoma, neoplasm, osteocarcoma;
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(WHIT-) WHITEHEAD INST BIOMED RE.
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              22-0CT-1990 (first entry)
                                                  Human retinoblastoma gene.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       developing the disease.
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à ć	1333	AGANGTACATCTCAGAATCTTCATTCTGGAAVAAALLGACTIIGGAAGAATGGAATGGAATGAAAAAAAAAAAAAAA
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oy Gb	1873 2038	ATCTGGACCCTTTTCCAGCACACCCTGCAGAATGAASTAGAACTCATGAGAACAAGAACAACTTATTTT 1942
Oy Dp	1933 2098	TTGGACCAAATTATGATGTGTTCCALGTALGGAAAGTGAAGAAAAAAAATTT 1942
o o	1993 2158	AAATTCAAAATCALTGITAACAAGATALAGAGGAGGTEGTGAGGGGGGGGGGGGGAGGGAGGGGGGGG
ć d	2053 2218	AAACGIGITIIGAICAAASAASAASAATAEATETAITAIACHEEFTAIAAA EGGGG 2112
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**1 * CAGAATGTAAAAGAACTTACTGATTATTTTCTTCATCCAACTTATGTTTTAAATGAGG 3372*
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3548
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ABROGGT Standard, cDNA, 4740 BP.

31 1383 ABKBBBB

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anticancer agent is used for the treatment of cancers such as breast bladder, skin, stomach, liver, colon and oral cavity, lymphoma and leukacharia. The anticancer agent induces apoptotic death, of cancer cells and the Rb inhibitor increases the apoptosis inducing activity of myoclacion even in Ph-positive cancer cells. The agent is specific to
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          myroramings even in Phippsilive cancer cells. The agent is specific to cancers in which Rb proteins are optionally expressed and myrolactone
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         122 CGGAGGACCTGCTCTCGTCAGGCTTGAGTTTGAAGAAACAGAAGCAGATTTTACTG 181
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   The invention relates to an anticancer agent comprising myrolactone. Also included for is as anticancer agent comprising myrolactone and antisense inhibitors of relinoblastoma (Rb) protein expression. The
                                                                                                                                                                                                                                                       Haman, relinchlactors protein, RL, cytostatic, cancer; apoptosis;
mycolactone; antisense; breast cancer; bladder cancer; skin cancer;
stowach cancer; liver cancer; colon cancer, etal carity cancer;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                shows very strong antibaneer effect in sitto us well as in vivo. The present sequence is the human cDNA for retinoblastoma protein.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          194 AARRORGGGRARRORGEDERPROGESTOOTECTBAGGAGGAGGAGGAGGAGGARAVACCCCTT
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Anticancer agent useful for treatment of cancer e.g. of skin,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Sequence 4740 BP; 1508 A; 887 C; 862 G; 1483 1; 0 other;
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                                                                                                                                                                                Human retinoblastoma protein cDNA sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Ċ
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Example 4; Page 38-42; 44pp; English.
                                                                                                                                                                                                                                                                                                                                                                        lymphoma; leukaemia; gene; ss.
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22-NEV 2000, 2000KR-0080184.
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osteosarcoma, fibrosarcoma, soft tissue sarcoma, small cell sarcoma,
esp. of the lung, melanoma and mammary tumours.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      DB 9; Length 4579;
                                                                                                                                                                                                                                                                                                                                                             Detecting pre-disposition to develop— using retinoblastoma gene probes to detect defects in the retinoblastoma.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Sequence 4579 BP; 1477 A; 843 C; 808 G; 1451 T; 0 other;
                                                                                                                                                                                                                                                                                                        Fung YKT, T'Ang A, Murphree LA, Benedict WF;
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94.4%; Pred. No. 0;
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                                                                                                                             Probe, retinoblactoma, tumbur; ss.
            AAN81261 standard; cDNA; 4579 BP.
                                                                                                                                                                                                                                                                                                                                                                                                          Claim 14; Page 17; 32pp; English.
                                                                                                 Probe for retinoblastoma gene.
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3	152	** TIGATIVISAAN'NATITOTOTICCATOTOTOTOTAAAAAGC	1410
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2311 ACTCCAAGATCAAGAATCTTAGTATCAATTGGTGAATCATTGGGGACTTCTGAGAATTG 2370 2.371 CAGAAAATAAATCAGATGGTATGTAACAGGGACGTGTGCTGTGAAAAGAAGTGCTGTGAGGA 24.30 1560 TITGAITITIACAAAGIGAICGAAAGITITAICAAAGAAGAAGAAGITGA AAGAGAA 1619 1591 CTICAATO IOCTIGICO LA BAICTICCIO COGABALAAICAVACACAGATAIG 1650 1651 TATCITICICIGIAAGAFCICGAAAGAAAAAAGIICAACIAAAGGIGGAAAITCIACI 1710 1771 TOTOTITICACTOTITIATAAAAAGTGTATOOOTTAOOTTATOOOTTAAATAOAOTT THAO 1951 IGTTCCATGTATGCCATATGCAAAGTGAAGAATATAGAACTTAAATTCAAAATGATTGTA 2010 2071 GANGAGGAGIATGATTATTATAGTATTCTATAACTCGGTCTTCATGCAGAACTGAAA 2130 2459 ACTOCANGATOAAGATOTTAGTATOATTGGTGAALOALOGGGAOTTOTGAGAAGTEC 2518 2431 AGCAACCTCCTAAAACCACTGAAAAAACTACGCTTTGATATTGAAGGATCAGATGAAGCA 2430 1471 ATGATAAAACATTTAGAACGATGTGAACATCGAAFCATGGAATCCCTTGCALGGCTCTCA 1530 1831 TGTGAACGCCTTCTGTCTGAGCACCCAGAATTAGAACATATCATCTGGACCCTTTTCCAG 1890 1891 CACACCTGCAGAATGAGTATGAACTCATGAGAGAGAGGATTTGGGACCAAATTATGATG 1950 2100 TGTTCCATGTATGGCATATGCAAAGTGAAGAATATAGACTTAAATTCAAAATGATTGTA 2159 2399 ATTTCACCCCTGAAGAGTCCATATAAAATTTCAGAAGGTCTGCCAACAACAAAAATG 2458 2491 GATGGAAGTAAACAFCTEECAGGAGAGTCCAAATTTCACCAGAAACTGGCAGAATGACT 2550 1411 TITGATITITIAGAAAGIGALGGAAGITITIALGAAAGPAGAAGGYAACLIGAYAAGAAA 1470 2579 AGCAACCCTCCTAAACCACTGAAAAACTACCTTTGATATTGAAGGTCAGATGAAGG FILLER FERRENCE FOR THE 2160 ACAGCALACAAGGALCLICCICAIGCIGITCAGGACA ALICAAACILI GALCAAA 2280 ACAAATATTTGCAGTATGCTTCCACCAGGCCCCCTTACCTTG -CACCAATACTCACATT 2011 ACAGCATACAAGGATCTICCICAIGCIGIICAGGAGACATICAAACGIGTTIGAAA 2131 ACAAATATITIGGAGTATGCTTCCACCACCCCCTACCTACTTGTCACCAAACTTACATT 2191 CCTCGAAGCCCTIACAAGITECCIAGITCACCTIACGGALLCTGGAGGAAAATTAT λο --q a ò 9 ŝ g ò = Ś 2 ŝ 9 ò 9 ŝ 3 ć 9 Š <u>a</u> ŝ 2 à 9 S g ò 3 ŝ 8 ô

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Meditiod retinoblastoma tumour suppressor, RTSP protein, cancer therapy;
                                                                                                                                                                                                   2500 COLAMINGAANAORAA HOMAAAHMAGAAAA GAATGAATGATGGATGGATGGATGGATGGAAGAAG 2610
                                                                                                                                                                                                                                                                                                                                                                                                      2600 TETACTEGAACACGAATGCAAAAGCAGAAATGAATGATAGCATGGATACETCAAACAAG 2758
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2433 JASTERSANDIAAACAICICCCAGRAAAATTTOAAAIITTOAGASAAACIGGCAGAAAIGACI 2698
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This sequence encodes a modified tetinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting callular prollieration, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular prollieration, particularly cancers. The RISPs have a broader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         348 GTTCACTTTTTACTGAGGTACAGAAAAAGTAGAAAICAGTGCGTAAAATTGTLLIAAGTT 407
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                468 GTATGATGTATTGTT1GCACTGTTCAGCAAATTGGAAAGGACATGTGAAGTTAFATATTT 527
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         408 ACTABARGADA FIGATACCAGIACCADA GALGAIA DE LA COLA TELEBAGA COLE FEDAGA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Match 91.3%; Score 3088.6; DB 19; Length 4455; Local Similarity 94.9%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                               Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Sequence 3455 BP; 1153 A; 631 C; 627 G; 1044 I; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              0; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                              Claim 22; Page 142-147; 249pp; English.
                               Location/Qualifiers
                                                                                                                                                                                                                                                                               Xu H, Zhou Y;
                                                                                                                                                                                                                           (BAYU ) BAYLOR COLLEGE MEDICINE (TEXA ) UNIV FEXAS SYSTEM.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            activity than wild type RTSPs.
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Homo sapiens.
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ŝ	1017	TCAA/CTTCAGAAAATCTGATTTCCTATTTTAACAACTGCAGGGAATGAAT	1076	
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1868 1557 ACAATCAAAGGACCGAGGACCAACTGATCACTTGAATCTGTTGCTTGTTTAATCT 1616 1677 GAAAAAAGGITCAACIAGGGIGIAAAIICIACIGGAAAIGGAGAGAGAGACACAACCTC 1736 1569 ACATCCAATCATGCAATCCTTTCCATGCTTCTCAGATTCACTTTATTGATCTTATTAA 1528 1617 ICCICICCAGAMAATCACACACACACATATCHATCHITCHCTCHMAAGALCHCTAAAA 1689 TCCTCTCCAGAATAATCACACTGCAGGAGAIATGTATGTTTGTCCTGTAAGATCTCCAAAA 1737 AGCCTTCCAGAGCCAGAGGCATTGAAATCTACCTCTCTTTCACTGTTTTATAAAAAGT 1809 AGCCTTCCAGACCCAGAAGCATTGAAATCTACCTCTTTCACTGTTTTATAAAAAAG 1797 GTATCGGCTAGCCTATCTCGGCTAAATACACTTTGTGAACGCTTTCTCTCAGCCC 1857 AGAATTAGAACATATCATCTGGACCCTILLIC AGCACAC CLOCAGAALGAGIAIGAACT 1917 CATGAGAGACAGCATTTGGACCAAATTATGATGTTCCATGTATGGCATATGCAAAGT 1977 GAAGAATATAGACCTTAAATICAAAATCALIGIAAMAMATAMAAAGALCTIRCIMATGM 2049 GAAGAATATAGACCTTAAATTCAAAATCATGGTAACAGGATACAAGGATCTTCCTCATGC 2097 ATTCIATAACTCGGTCTTCAIGCAGAGACTGAAAAAAAATATTTGCAGTATATGCTTCCAC 2169 ATTCLATARCIGGGTCTICATGGARARGACIGAAAAAAAATATTTGGAGAGATGTGCAACAACAA 2229 CAGGCCCCTACCTTGTCACCAATACCTCACATTCCTCGAAGCCCTTACAAGTTTCCTAG 2217 ITCACCCTIACGGATICCIGGAGGGAACAICIAIAIITCACCCCTGAAGAGICCAIATAA 2349 AATTICAGAAGGTCTGCCAACACAACAAAAATGACTCCAAGATCAAGAATCTTAGTATC 2.3.3. AATITGGTGAATGATITGGGGAGTTCTGAGAAGTTCGAAAAATAAA FCAGAATGATAA 2397 CAGCGACCGTGTGTCAAAAGAAGTGCTGAAGGAAGCAACCATCCTAAAAAA ACTACGCTTTGATATTGAAGGATCAGATGAAGCAGAGAGAAGTAAACATCTCCCAGGAGA 2529 ACTACGCTTTGATATTGAAGGATCAGATGAAGCAGATGGAAGTAAACATCTCCCAGGAGA 2517 GTCCAAATTTCAGGAGAAAGTGGGAGAAATGATTFTAGTGGAAGAGAAAGGAA 2589 GTCCAAATTTCAGCAGAAAACTGGCAGAAATGACTTCTACTCGAACACAAAGGA 2037 TOTICAGGAGATICAAACGIGITTIGATCAAAGAAGAGAGTATGATIGIATATAAA 2457 ŝ qq ã ŝ g 음 ó qq ŝ 9 ŝ q င် g <u>a</u> a ò qq q â ò q a d 2 ŝ ŝ ŝ ŝ ò ŝ ŝ ŝ ò g ò

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24.47 EBBTGGAVANTGTGTAGAGTGTGAGATTGATGTGTGTGAGAGATGTGAGAGTGTATAACTT 2696
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This sequence encodes a modified retinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The KISPs can be used for treating diseases characterized by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           352 ACTITITACTGAGCTACAGAAAACATAGAAATCAGTGTCCATAAATTCTTTAACTTACTA 411
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Match 89.4%; Score 3024.6; DB 19; Length 3392; Local Similarity 94.8%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                              Retinoblastoma suppressor protein with N·terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Sequence 3392 BP; 1137 A; 614 C; 607 G; 1034 I; 0 other;
                                                                                                                                                                                                                                                                                                                                                 inhibiting cellular proliferation, particularly cancer
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ολ	1681	681 AAAQQTICAACIACGGIGIAAATICTATIGAAAQQAGAAAAGAAAAAAAAAAAAAAAAAAAAAAA
qq	1690	AAAGGTECAACTAGGGGGGTGTAAATTGTACTGTAAATGCAGAGAGACAAAAAAAA
ò	1741	TTCCAGACCCAGGAAGCCATTGAAATCTACCTCTTTCACTGTTTTATAAAAAAGTGTAT 1800
qq	1750	TTCCAGACCCAGAAGCCATTGAAATCTACCTCTTTCACTCTTTATAAAAAAGTGTAT 1809
ò	1801	COGCTAGOCTALCTCCCGG/CTAAATA/A 111 GAGAAA/GCTILCTGTCTGAGAA OCAGAA 1860
qa	1810	CGGCTAGCCTATCTCCCGGCTAAATACACTTTGTGAACGCCTTCTGTGAGCACCAGAA 1869
ογ	1861	TTAGAACATATCATCTGGACCTTTTTCCAGCACACTGCAGAAGAGTGAGAACTGGAGAACTG 1920
qq	1870	TTAGAACATATCATCTGGACCCTTTTCCAGCACACCTGCAGAATGAGTATGAACTCATG 1929
QY	1921	AGASACASSCATTISGACGAAATTATGATGTEGGAGGTAIGGAAAAAGAA 1980
q	1930	AGAÇAÇABITIRIN ÇERÇEYAATTATOATGITECATĞI ALTITIKLI ILLI ILLI ILLI ILLI ILLI ILLI I
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qa	1990	AATATAGACCITAAATICAAAATCATGIAACAGCATACAAGATCATGITTICTICTICTICTICTICTICTICTICTICTICTICTI
О.	2041	CAGGAGACATICAAAGGIGITIIGAICAAAGAAGAGGAGTAIGAIICIAIIAIATIC 2100
qq ;	2050	CAGGAGACATICAAAGGTGTTTGATCAAAGAAGAGGAGTATGATTGTATTATATATTC 2109
λο :	2101	TATAACTCGGTCTTCATGCAGACTGAAAACAAATTTTGCAGTATGCTTCCACAGG 2160
qu	2110	TATAACTCGGTCTTCATGCAGAGACTGAAAATTTTTTTTT
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qd	2170	CCCCCTACCTTGTCACTCACTCACATACTCCTCGAANGCCTTACAAGTTTCCTACTTCA 2229
ογ	2221	CCCTTACCGATTCCTCCTCCACCCAAATCTATATTTCACCCTCAACACTCTATATAAAATT
qq	2230	COCTTACGGATTCCTGGAGGGAACATCTATATTTCACGCGGAAGAGGGGATATAAAATT
ΩY	2281	TCAGAAGGTCTGCCAACACCAAAAAATGACTCCAACATCAACAACATTACTTAC
DD	2290	I CAGAAGU CI GCCAACAACAAAAA GACI CCAAGA I CAAGAA CTI ACI AATI
ç	2341	GGTGAATCATTCGGGACTTCTGAGAAGTTCCAGAAAATAAAT
qq	2350	GGTGAATCATTCGGGGACTTCTGAGAAGTTCCAGAAAATAAAT
Óγ	2401	GACCOLG TORICAAAGAAGTGCLGAAGCAACCACCOLOCTAAACTAAAAAAAAAAAAAAAAAAAAAA
qu	2410	GACCGTGTGCTCAAAAGAAGGCTGAAGGAAGCTAAAAAAAA
Ογ	2461	CGCTTTGATATTGAAGGATCAGATGAAGGAGATGAAACATCTCCCAGGAGGTCC
qa	2470	COCITITIGATATITGAAGGATFAGATGAAGFAGGAAGTAAAFATFT CCFACGAGAGTG
ćλ	2521	AAATTTCAGCAGAAACTGGCAGAAATGA" 11 FT TACTCGAAC A'GAATGCAAAAGAAAA
qq	2530	AAATTICAGCAGAAACTGGCAGAAATGACTTCTACTCGAACACGAATGCAAAAAGCAGAAA
ογ	2581	ATGAATGA TAGCATGGA FACCTCAAACAAGGAAGAAA TGAGGA LTTAGGACTTTGT
qq	2590	ATGAATGATAGCATGCATCATCAAACAAGAAGAAAATGAATG
ć	2641	GGACACTGTGTACACTCTGGATTGTCTCCCCCAAAGATGTATAAATAA
qu	2650	60ACACTGTGTACACCTCTGGATTCATTGTCTCTCACATGTCACTGTATACTTTTCC 2709
ογ	2701	AGGITCIGITIAIGGCCACATITAATATCITCACCITITTGGGATATAAAARGGCA 2760
O.C.	2710	AGGITCIGITIATGGCCACATITAATATCITCAGCTCITITGTGGATATAAAATGTGCA 2269
ΟY	2761	GATGCAALTGTTTGGGTGALTCCTAAGGCACLTGAAALGTLAGTGALTGTTALTATACA 2820

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Ç.	u*00 00.1	2		e Ci	AB1.12861	brosophila melanoa

ALIGNMENTS

PESULT 1

Meditied retinoblastoma tomour suppressor; RISP protein; cancer therapy; Modified retinoblastoma tumeur suppressor gene. sellular proliteration inhibitor, ss. Location/Qualifiers AAV58446 standard; DNA, 3323 BP. 02-DEC-1998 (first entry) 7..2562 Home sapiens AAV58446; AAV58446

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protein (RISP) of the invention. The proteins can be used for inhibiting coliular proliferation, when enadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            proliferation, particularly cancers. The RISEs have a broader spectrum of activity than wild type RISEs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           81 LeupheAlaLeuPheSerLysLeuGluArqThrCysGluLeuIleTyrLeuThrGlnPro 100
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              This sequence encodes a modified retinoblastoma fumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                   Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Sequence 3323 BP; 1099 A; 647 C; 588 G; 989 T; 0 other,
                                                                                                                                                                                                                                                                                                                                                                                                                          inhibiting ceilular proliferation, particularly cancer
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                                                487 CCATATAAAACAGCIGIIAIACCCAITAAIGGIICAC ICGAAGAGCCAGGGGAGGICAG 546
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Modified retinoblastoma tumour suppressor: RISP protein; cancer therapy;

Modified retinoblastoma tumour suppressor deme.

02-DEC-1998 (first entry)

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protein (RTSP) of the invention. The proteins can be used for inhibiting celular proliferation, when coadministered with a p54 protein. The RTSPs can be used for treating diseases characterised by abnounal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
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                                                                                                                                                                                                                                                                                                                                     Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 3461 BP; 1141 A. 675 C. 627 G; 1018 T; 0 other;
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protein RH (see AAM62465). A new claimed polypeptide is a fusion of:
(i) a transcription factor (IF) comprising a DNA binding domain,
and (ii) a retinoblastomma (Rb) polypeptide that includes a growth
suppression domain. Also new are: (1) a nucleic acid encoding the
fusion protein, and (2) expression vectors containing such DNA.
The fusion protein, particularly expressed from gene therapy HTTTFTHTHTHTHTHTHTHTHTHTHTH 259 GACCOGOCICING INGOINAGE IN TRANSPACACAGAGAGAGCON GALLITACTICATOR 318 379 GITTCATGIGGAIGGAGIATIGGGAGGITATATATICAAAAGAAAAAGGAACTGIGGGGA 438 319 1010740AAATTAAAGATACCAGATGATGTCAGAGAGAGGTTGGTTAACTTGGGAGAAA 378 vascular disease. Tissue specific expression of E2F-PR factors is provided. The fusion proteins are more effective in repressing transcription of the E2F promoter than Rb alone and cause cell-cycle. 1 Met ProproLysThrProArgLysThrAlaAlaThrAlaAlaAlaAlaAlaAlaGluPro 20 This nucleotide sequence includes a coding region for retinoblastoma vectors (especially ademovirus vectors), is used to treat the properties of the properties of the properties of the properties of the bladder) or restenosis (after angloplasty), but also diabetic retinopathy, thyroid hyperplasia, Grave's disease, psociasts, retinopathy. peniqu prostatic hypertrophy, Li-Fraumeni syndrome and peripheral New fusion polypeptide of, e.g. franscription factor - used to freat, e.g. hyper-proliferative disease such as cancer and Sequence 2994 BP: 974 A: 618 C: 593 G: 809 T: 0 other; Conservative: Mismatches: 21 ProAlaProProProProProProProGlu-----Matches: Length: Indels US 09 026 459A 39 (1 851) x AAV40004 (1-2994) WILLS KN; Example 1: Fiq 2A: 91pp: English. arrest in a variety of cells. 97WO - US21821. 970S 0801092 96US 0751517 4 1 1 1 5 0 91.70**%** 91.70**%** 38.85 Antelman D. Gregory KJ. WP1; 1998 297858/26. (CANJ) CANJI INC. vascular disease. Percent Similarity: Rest Local Similarity: P PSDB; AAW62465 13 NOV 1997; 15 Nov 1996; Allemment Scores: W179821228 A1 14 FEB 1997; 8561 AVM 77 restenosis provided. Querry Match: ₽ <u>.</u> ĩ 3 3 <u>:-</u> 2 ŝ 5

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This sequence represents the wild type human retinoniastoms as us. The invention relates to a method of detecting a mutated retinoblastoms (mRP) norther actif in mammals comprising hybritising at solated full-length, wild-type RB (wtRH) conserve a cell sample and detecting a mutated RB nucleic acid. The method is useful as a diagnostic fool for diagnosing retinoblastoms PR PNN or genomic INA are preferably used as probes to determine the detect region of the mRB gene through used as probes to determine the detect region of the mRB gene through among INA but ing analysis or using the allocased alleic. Cloned RB
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       RB gene; human; retinoblastoma gene; mutation detection; immunoscreening; retinoblastoma dayanesis, hereditary retinoblastoma; secondary cancer; osteosarcoma; fibrosarcoma; glioblastoma; breast cancer; tumourigenesis suppression; sa
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   CONA can be used to generate specific anti RB protein (anti-ppkH)10) anti-ppkH)10 a
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764 ThrSerSlatysDbcClntysDcAsnClnMctValCysAsnScrAspArgValLentys 783
                                                                                                                                                                                                                                                                                                                                                                                        824 LeualadlumetThrSerThrArgThrArgMetClnLysClnLysMetAsnAspSerMet 843
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cancer whether or not connected with retinoblastoma. The method is also used in the suppression of tumouridenceis where the absent RB protein parklib will be provided through the molecular induction and genetians transplanting of the RB cDNA to the individual in need of ppRHIIO.

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The present invention describes a composition comprising a recombinant adenovirus expression vector, where the vector has an insert of exogenous DNA comprising a gene encoding a toration protein and adenovirus DNA in which all of the coding sequences of Ela, Elb, and protein IX, and part of El are deleted. The vectors are useful in gene though treatment of cancer, especially for treating p53 deficient tumours. The vector enables saler and more efficient gene therapy of cancer. The present sequence encodes human p119. RB retinoblastoms tumour suppressor which can be used as the loreign gene in the above
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         259 GACCTGCCTCTGGTCAGGCTTGAGTTTGAAGAACAGAAGCAGATTTTACTGCATTA (18
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                                                                                             /note- "retinoblastoma tumour suppressor"
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                                         Location/Qualifiers
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7	gleuAsnThrieuCysGluArgleoikeuSerGluHisProGluikeuCluHisTlette 	603 2178
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Oy 724 G1	yGlyAsnIloTyrIleSerFrolestynSerFroTyrLysIleSerGludlyLeuFro 	743

0 other;

Sequence 2995 HP; 475 A; 618 C; 593 C; 209 T;

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Recombinant adenovirus expression vector comprising a partial or total deletion of a protein IX DNA and a gene encoding a foreign protein e.g. suicide protein, useful for inhibiting or reducing the proiferation of
                                                               8.4 GlySerAap "JA'aAap" ySerJysEfs' euDreGlyClySerJysDycClySerJys 823
744 Thritopherysmorthronardsgararillet...(Sarther) vg1uSrephally 763
                                                    764 ThrserGlutjaFheSlatjaIleAanSluMetValOjsAsuSerAspArgValLeutjs 783
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                                                                                                                                                                                                            824 LeuAlaGluMetThrSerThrArqThrArqMetGlnLysClnLysMetAsnAspSerMet 843
             Refinablastama, tamon, suppressor profess; Rb, p53; cancer; adenoviral vector; gene therapy; thymidine kinase; ds.
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The present invention describes an adenoviral expression vector comprising a deletion in the protein IX gene and a gene encoding a foreign protein. This vector can be used in gene therapy, particularly to introduce tumour suppressor genes into camperous cells. Genes which may be used include p53, thymidine kinase and retinoblastoma tumour suppressor dene (kb). The present sequence is the retinoblastoma tumour

suppressor gene.

Disclosure; Fig 3; 39pp; English.

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979 CATGAATGTAATATAGATGAGGTGAAAAATGTTTATTTGAAAAATTTTATACTTTTATAG 1038
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cytostatic, antithyroid, antipsoriatic; adenovial protein IX; psoriasis; thyroid hyperplasis, thave's disease; hepdrocelular carethoma; neoplasm; benign prostatic hypertrophy. Li Frammen syndome; sickle cell anaemia; Tay Sachs disease, leukaemia, lymphoma, adenovina, ector, camer; ss.
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2119 CGGCTAAATTACACTTTGTGAACCCCCTTCTGTCTGACCACAAATTAGAACATATATC 2178
                            604 TrpThrLeuPheGluHisThrLeuGlnAsnGluTyrGluLeuMetArqAspArqHisLeu 623
                                                                                                                                                  644 PheLysilelleValThrAlaTyrLysAspLeuProHisAlaValGluGluThrPheLys 664
                                                                                                                                                                                                              664 ArqValLeuIleLysGluGluGluTyrAspSerIleIleValPheTyrAsuSerValPhe 683
                                                                                                                                                                                                                                                                     684 MetGluArqLeuLysThrAsnlleLeuGlnTyrAlaSerThrArqProProThTLeuSer 703
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                                                                                       624 AspCln1leMetMetCysSerMcTTyrClylleCystysVallysAsn1leAspLenHys
                                                                                                                                                                                                                            824 LeuAlaGluMetThrSerThrArgThrArgMetGlnLysGlnLysMetAsnAspSerMet
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1392925 7*iour a 7riour "ketinobiastoma tumour suppressor protein. p11088"	0939-81.	R-2001.	1-1994; 94US-0328673.	T-1993; 93US-0142669. Y-1994; 94US-0293777	CANST INC.	ry 8J, wills KN, Manegal DC;	WET: 2001 DB9433730. P. PSDB: AAE00689.	New recombinant ademovirus expression vector having a gene encoding for a foreign protein and a partial or total deletion of the ademoviral protein IX DNA, useful in gene therapy for treating or reducing hyperproliferative cells.	osurer Eig 3: 49pp; English.	The present CDNA sequence encodes refinebiastown (PR) tumour suppressor protein, designated as plloks. The investion relates to a recombinant adenovirus expression vector that actual related by the partial or fotal deletion of the adenoviral protein IX inva beginning at muciontides 457 or 455 and partial at 452 455, and harring a gene encoding a foreign protein such as tumour suppressor protein, plloks (refinebiastown) and p53. Adenovirus vector is used to screening tumour suppressor genes useful in gene therapy. The vector is protein, plantly useful treating or reducing hyperprofilerative cell disorders such as thyroid hyperplasia, Grave's disease, psociasis, benian prostatic hypertrophy, id Fraumeni syndrome, caucers specifically heptocellular carcinoma, nooplasms, leukaemias, lymphomas, etc. to faithology such as sickle cell anaemia and Tay-Sachs disease. The vector is also useful for the safe recombinant production of diagnostic and tay-berapeutic polypeptides and productions.	Sequence 2995 BP; 975 A; 618 C; 593 G; 809 T; 0 other;	Scores: A 33.50 Matches: ### ### ############################	459A-39 (1-851) x AAD04474 (1-2995)	Met Profrojt of ysfibriproargi ysfibrafaalaafaafaafaafaafaafaafaafacoppro-20 	ProAlaProProProProProProProGlu	
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2y 3b	4 0	ThrileGloGloLecMctMctIleteuAspSerAlaSerAspGloFroSerSiuAspLe. 323 [HIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	323
23.	Č	: CSGrTyrPbcAsnAsnCysTbrVa:AsnBrctcQysGluGcrTilcLcUgsArgVaHtys	343
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Retinoblastoma; tumour suppressor protein; pll0-RH; cell cycle; p53; Rb; mitosin; cell death; adenoviral protein IX; qene therapy; cytostatic; adenovirus expression vector; tumour; non-small cell lung cancer; small cell lung cancer; small cell lung cancer; hepatocarchinoma; hopatocellular carchinoma; melanoma; retinoblastoma; colorectal carchinoma; sarcona; Wilm's tumour; astroytoma; qlibblastoma; neuroblastoma; ovarian carchinoma;
                                                                                                                                        2539 GGAGGGAACATCTATATTTCACCCTGAAGAGTCCATAIAIAAAALLICAGAAGGLCGCCA 2598
                            744 ThrProThrLysMetThrProArgSerArglTeLeuValSerTleSlyCluserPheCly
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 /product- "retinoblastoma tumour suppressor protein"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      New recombinant adenovital vector comprising a partial or total deletion of a protein (X :NAA and a gene encoding a foreign profein, useful in gene therapy, particularly for freating or suppressing
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Retinoblastoma tumour suppressor protein pil0-RB encoding cDNA.
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The present invention describes a recombinant adenovirus expression vector, which comprises a partial or total deletion of a protein IX BNA and a gence encoding a foreign protein. The recombinant adenovirus vector can have expression vector is particularly useful for treating or suppressing proliteration of a tumour, a q non-small cell lung cancer, hepatocarchoma or hepatocalcular carcinoma, melanoma, retinoblastoma, breast rumour, colorectal carcinoma, pressate tumour, bladder tumour, tumour of the reticuloendothelial fissues, wilm's tumour, astrony, overian estimout, astrony or renal cancer. The present, sequence encodes the retinoblastoma tennous superessor protein plights, which is quiven in the exemplification of the present invention. Nishlosure; Fig 3; 37pp; English. presidentation of a tumor -

Sequence 2995 BP; 975 A; 618 C; 593 G; 809 T; 0 other;

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ą	-		AAATCAGTGCCATAA	AATTCTTTAACTTACT	CAGAAAAACATAGAAATGAGTGTGCGATAAAATTGTTTAAGTTACTAAAAAGAAATTGATAGC	558
3: 5	73	SerThrLysValA	spAsnAlaMetSerAr	rgLeuLeuLysLysTy	SerThrLysValAspAsnAlaMetSerArgLeuLeuLysLysTyrAspValLeuPheAla	83
ä	644		ATAATGCTATGTCAAG	3ACTGTTGAAGAAGTR	AGTACCAAAGTTGATAATGCTATGTCAAGACTGTTGAAGAAGTATGATGTTTGTT	618

| 124 | AlatysolygloValleuGlametGluAspAspLeuValleSerPheGlaLeumetLeum 143 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 11111 | 111

679 AINTCINCTACAAATAAATTCTGCAATTGGTGCTAAAAAGTTTCTTGGATCACAITTTTATTA 738

194 HoSerThrGlulleAsnSerAlabeuValbeubysVaiSerTrpHeFFFFFFLeubeu 123

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84 LeuPheSerLysLeuGluArqThrCysGluLeuIleTyrLeuThrGlnProSerSer 103

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0 <i>y</i> .	Н	HAVATERS HTHHHH SAGTGAAG	343 1398
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Q Op	-	spArgGlu FELLETT ACCGAGAA	503

AAV58440 standard; DNA; 4555 BP

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4479 CYAFAROTOACATICCTCGAAGCOTTACAAGITTCCTAGITCCCTAAGGTTCCCT 2548
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RESULT TO

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This sequence encodes a modified retinoblastoma tument suppresson protein (RISP) of the invention. The proteins can be used for inhibiting cellular proliteration, when coadministered with a p5+ protein. The PTSPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The PTSPs have a broader spectrum of
                                                                                                                          Modified retinoblastoma tumour suppressor; RUSP protein; cancer therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           127 GACCTGCCTCTGGTGAGGTTTGAAGAAAAAGAAGAAGAAGTTTAATAGATTTA 186
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Mismatches:
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	124	.euVallleSerPheG]ni.euMetl.e 	143 666
	144	ProMetLeuLeuLysG 	163 726
ж д	164	ThrProArgArgGlyGlnAsnArgSe 	183 786
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	204	TyrPholysAs HILLLILL FATTTCAAAA	223
	45.7	20G1uValG1uAssLeuSer 	243 956
:	244	laArgic 	263 1026
	1027	SluthrGlnar 	283 1086
	1087	lisThrProValArgThrValMetAs 	303 1146
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1387 CTTAAATCAGAAGAAGGATTATCCATTCAAAATTTTAGCAAACTTCTGAALGACAAC 1687 CIIGCAIGGTOTOTOAGAIICAOOTITATIIGAICTIATIAAACAATCAAAGGACCGAGAA 1746 2107 GACCAAATTATGATGTGCATGTATGGCATATGCAAAGTGAAGAATATAGACTIAAA 2166 1627 AACTTGACAAGAGAAATGATAAAACATTTAGAACGAIGIGAACATGGAGATGAATGAIGGAAICC 1686 484 focalatribleuSeraspSerFroLeuPheAspl.culletysGlnScrt.ysAspArgGlu 503 444 LeuAsnLeuLysAlaPheAspPheTyrLysValIleGluSerPheIleLysAlaGluGly 463 504 GlyProThrAspHisLeuGluSerAlaCysProLeuAsnLeuProLeuGlnAsnAsnHis 523 524 ThrAlaAlaAspMetTyrLeuSerProValArqSerProLysLysLysGlySerThrThr 543 544 ArgValAsnScrThrAlaAsnAlaGluThrGlnAlaThrScrAlaPhcGlnThrGlnLys 563 564 ProbeulysSerThrSerLeuSerLeuPheTyrLysLysValTyrArgLeuAlaTyrLeu 583 704 ProlleProllislleProArgSerProTyrLysPheProSerSerProLeuArgllePro 723 LeuLysSerGluGluGluGluArgLeuSerIleGlnAsnPheSerLysLeuLeuAsnAspAsn 403 464 AsnLeuThrArgGluMetIleLysHisLeuGluArgCysGluHisArgIleMetGluSer 483 584 ArgLeuAsnThrLeuCysGluArgLeuLeuSerGluHisProGluLeuGluHisI]eI]e 603 604 TrpThrLeuPheGlnHisThrLeuGlnAsnGluTyrGluLeuMetArgAspArqHisLeu 623 624 AspGlnIleMetMetCysSerMetTyrGlyIleCysLysValLysAs::lleAspLeuLys 643 644 PheLysIleIleValThrAlaTyrLysAspLeuProHisAlaValGinGluThrFhcLys 663 724 CHydlyAsii Clefyr HleScrib chechys Serib chynnys HleSerdladlyneithol 743 IlePheHisMetSerLeuLeuAlaCysAlaLeuGluValValWetAlaIhrTyrSerArg 664 ArgValLeulleLysGluGluGluTyrAspSerllelleValPheTyrAsnSerValPhe 2167 TTCAAAATCAITGTAACAGCATACAAGGAIGTICCICATGCIGTICAGGAGACAIICAAA 2227 COTOTITICANGANGANGASGISTATOATTOTATATAGIATOTATANGTCTCTTC 684 MetGlnArgLeuLysThrAsnileLeuGlnTyrAlaSerThrArgProProThrLeuSer 384 qd ; g qq ò l)b ò qq ò q ó qq ŝ qq Ωy ò Ω q ò 3 ò 10 ò q ò g ŝ \overline{q} õ a οy q ó 3 ŝ ö

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2407 GGAGGGAGGACTIAIAITICAGGGCTGAAGAGTCGATATAAAATGTGAGAAGGCGGCA 2466
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                                                                                                                                                                                                                                                                                                                                                                                                                                            804 GPSGTASpGluAlaAspClySerlysHisLeuproGlyCluSerlysPheGlnGlnLys 823
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                824 LenAlaGluMetThrSerThrArgThrArgMetGlnLysGlnLysMetAsnAspSerMet 843
                                                                                       744 Thr ProThat; ys Met Thr ProArd Ser Ard Hellen Val Ser (1001) yelluser PheCly 763
                                                                                                                                                                                                        764 Thr SerGluLysPheGluLysIleAsnGluMetValCysAsnSerAspArqValLeuLys 783
                                                                                                                                                                                                                                                                                                                            284 ArgserAludludlySerAsmProProLysProLeuLysLysLeuArqPheAspIledlu 803
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Minimal promoter; tetracycline responsive expression vector; TREV;
Now tetracycline responsive expression vectors—used for the tightly controlled expression of genes, such as tumour suppressor
                                                                                                                      transcriptional transactivation domain; IID;
tetracycline repressor protein; ERP; tetracycline operator;
production; stable cell line; protein production;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           fumour suppressor protein; treatment; cancer; ss.
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The present sequence appears in the specification, which describes a tetracycline responsive expression vector (TKEV), which contains a sequence encoding a tusion protein comprising a transcriptional

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transactivation domain (TID) operatively attached to a tetracycline repressor protein (TRP), the first sequence operatively positioned downstream of a promoter, the vector also contains a clound site operatively positioned downstream of a basal promoter comprising a tetracycline operator. The TREVS can be used to produce stable cell lines in which gene expression is tightly regulated by tetracycline. They can be used for the production of proteins such as tumour suppressor profeins which can be used to the production of proteins such as tumour
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   27 GACCTGCCTCTCGCTCAGCCTTGAGTTTGAAGAACAGAAGAACATGATTTACTGCATTA 186
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                246
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             247 CTTTCATCTGTGGATGGAGTATTGGGAGGTTAFATTCAAAAGAAAAAAGAACTGTGGGGA 306
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              144 CysValLeuAspfyrPhelleLysLeuSerProProProMetLeuLeuLynGluProFyrLys 164
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                                                                                                                                                                                                                                                                                                                                                                                                                                                         1 MetProProLysThrPtoArgLysThrAlaAlaIhrAlaAlaAlaAlaAlaAlaAlaGluPto 20
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                                                                                                                                                                                                         Sequence 3555 BP; 1171 A; 684 C; 653 G; 1047 T; 0 other;
                                                                                                                                                                                                                                                                                                                Conservative:
Mismatches:
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Matchos:
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204	Hisglucysaspileaspoluvallysaasvaltyrpelysaspipheileprophemet.	
524	ASERSCITCOGLYLCOVATHITISCYASDCLYLCOPPOGLOVATGLUASDLCUGCTLYSAFG	243 966
545 545	Tyestandent etyrkonkygdsnkygdspkoudspaladrykoneuthendentiisasp + + + + + + + + + + + + + + + + + + +	263 1026
26.4 1927	Systhrie-dinthraspserlieaspserphediuthrdinargthrprodrgLysser and the state of the s	283 1086
284	AshlewaspiludluValAshValileProproHis"hrProValArgihrValMetash 	303 1146
1147	ThrileglusinieuMetMetileLeuAsnSerAlaSerAspGlnProSerSluAsnLeu 	323 1206
12.17	1 1 2 2 2 2 2 2 2	343 1266
1267	ASPILECTYTYTTEPHOLYSCIALYSPHOALALYSALAVALGLYCINCTYGYSVALGTU TITTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	
147	11-64]ySerGlnArgTyrLysLeuGlyValArgLeuTyrTyrArqValMetGluSerMet. 	∞ m
184	Leulysserfludludrqleuserfledinasnpheserlysleuleudsnaspasn (○ 4
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424	SerThriserGinasnLeunapRerGlyThrAspLeuSerPheProTrpIleLeunasnVal 	44 RC
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46.4	Asilienthranglumetilelystisieugtuargeyselütisargilemetelüser ELELLITITITITITITITITITITITITITITITITITI	483 1686
184	LeudlaTrpLeuSerAspSerProLeuPheAspLeuIleLysGlnSerLysAspArgGlu 111111111111111111111111111111111111	503 1746
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2107 GACCAAATTATGATGTGTTGCATGTATGGCATATGCAAAGTGAAGAATATAGACCTTAAA 2166
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                                             564 ProteutysSerThtScrieuSerLeaPheTyrtysUysValTyrArgleuAlaTyrLeu 583
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                                                                                                                                                  604 TrpThrLeuPhedlnHisThrLeuGlaAsaGluTyrGluLeuMetArqAspArqHisLeu 423
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544 ArgValAsnSerThrAlaAsnAlaGluThrGlnAlaThrSerAlaPheGlnThrGlnLys 563
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Human retinoblastoma gene.

hEST2: relomerase; catalytic subunit; reverse transcriptase; lite-span, returblastoma; p53; tumour suppressor; inhibitor; arteriosclerosis; proliteration; immortal; tumour therapy; macular degeneration; activator;

Homo sapiens.

W0200011248 AZ.

.000**7 N**HC 70

99W0-00027907. 24 NOV 1939; 25 NOV 1998;

9805-0109891. 9905-0120549. 17 FEB 1939;

(GENE) GENETICA INC.

Hannon G.I. Beach DH;

WP1; 2000 400055/14.

New method for increasing the prollierative capacity of cell lines comprises administration agents reversibly activating telumerase activity and reversibly increivating Rb/INK4 and/or p53 pathways useful in treating age related diseases.

Claim 5; Page 121 123; 123pp; English.

subsequently of use in pharmaceutical and cosmetic preparations used to treat conditions related to (premature) ageing, e.g. macular degeneration and attentosclerosis. The cells can also be used to replace tumour cell lines in vitro and the studies on biodemical and physiological aspects of growth and differentiation. Long lived (immortal) cells could also be used in the production of normal or genetically engineered e.g. the number of mitotic divisions, of a cell. The method relies on a divisition of a telementase activity and inhibition of one or both of a retinablastoma (Rb)/INK4 pathway of a p53 pathway. Phosphorylation of Rb by cyclin dependent Kinases, coff and coke, releases the cells into the division cycle. Binding of INK4 tamily members, e.g. the tumour suppressor plofikk4, inhibits kinase activity and results in growth arrest Rb inactivators can selectively and reversibly inactivate an Rb/LNK4 pathway, especially in RNY2 is a cellular inhibitor of Rb/E2F function and the p53 tumour suppressor The invention concerns methods and reagents for extending the lite-span, and can also be used in the methods. Other molecules which can be used include cake or cake amutants. In particular, a cake mutant is one which differs from at one or more of residues K22, R24, H95 and/or D97. Additional constructs include a papilloma virus E7 protein, or other p53. Antisense constructs of The methods are useful for viral oncoprotein which bypasses Rb and/or p53. Antiscuse consitie Rb and p151NK4a genes may also be used. The methods are us increasing the proliferative capacity of cells. The cells are biotechnology products.

Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other;

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Pred. No.:	0	Longth:	4839
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Novel androgen receptor associated proteins used to detect androgenic or antiandroquaic activity in screening assays for candidate pharmaceutical molecules which promote or inhibit the activity

laim 8: Page 47 54; 59pp; English,

designated Rb. Androgen receptor co-activator proteins from the present invention can be used in streening assays to identify candidate pharmacentical molecules for the ability to promote or inhibit the interaction of androgen receptors and androgen responsive elements to modulate androgen receptors and androgen responsive elements to include androgenic activity. The identification and characterisation of anorogenic receptor co-activity as such as those of the invention will terilitate the development of screening assays to evaluate the potential The present sequence encodes a human androgen receptor coactivator efficacy of drugs in the treatment of prostate cancer.

Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 F; 0 other;

Conservative: Mismatches: Indels: Matches: Lengt h: Gaps: 4 3 1 3 , 50 91.70**%** 91.70**%** 98.893 Best Local Similarity: Percent Similarity: Aliqument Scores: Pred. No.: ouery Match: bb:

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11HTHTHTHTHTHTHTHTHTHTHTHTH 104 TleSerThrGluffeAsnSerAlaLeuValLeufysValSerTrpffeThrPheLeuteu 123 84 LeuPheSerLysLeuGluArqThrCysGluLeuIleTyrLeuThrGluProSerSer 103 478 OTTTOATOTOGGATGGAGTAFTGGGAGGTFAFATTCAAAAGGAAAAGGAACTGTGGGGA 437 44 elidysAsnileGinileSerValHistysPhePhePheAsnieuLoutysGinileAspihr 63 30 ---ValAspLeuAspGluMetSerPheThrPheThrGluLeu 43 64 SetThtLysValAspAshAlaMetSetArgleufentystysTyrAspValLaupheAla 83 1 MetProprobysThrProArqLysThrAlaAlaThrAlaAlaAlaAlaAlaGlupro 20 21 ProAlaProProProProProProProGlu-----**9** Ξ 5 £ 5 <u>2</u> 5 ÷ 5 ŝ S Ξ 5 5 5 5 ŝ

144 CysValLeuAspTyrPheIleLysLeuSerProProMetLeuLysGluProTyrLys 163

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ąq	798	TGTGTCTTGTTTTTTTTATTAAGTCTCACCTCCCATGTTGCTCAAAGAACCATATAAA	857
οy	164	ThratavaliteprofleasnGlySerProarqfhrProarqarqGlyGlnAshataSer	Ŧ.
qq	858	ACAGCTGTTATACCCATTAATGGTTCACCTCGAACACCCAGGGCGAGGTCAGAACAGGT	417
ò	184	AlaArqileAlaLysGluIsuGluAsnAspThrArqileIleGluValLeur'ysLysGlu	107
qq	918	GCACGGATAGCAAAACAACTAGAAAATGATACAAAAATTATTGAAGTTCTCTGTAAAGAA	477
Ġ.	ី	284 HisologysAsnileAsFolyValLysAsnValTyrFhelysAsaEheileFicMet 223 HIBBERTHEHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	* * * * * * * * * * * * * * * * * * *
qq	978	CATGAATGTAATAGATGAGGGGGAAAAAGGTTTATTTCAAAAATTTTATGTTTTATG	1037
07.	₹ (1	AsnSert.euClyt.euValThrSerAsnClyt.euDro.21.uValCluAsn.2-uSert.ysArq	243
qq	1038	AATICTCTTGGACTTGTAACATCTAATGGACTTCCAGAGGTTGAAAATCTTTCTAAACGA	1097
ó.	244	TyrGluGlullefyrLeuLysAsnLysAspLeaAcpAlaArqLeuPheLeaAspHisAsp	197
. Q	1098	TACGAAGAAATTTATGTTAAAAATAAAGATCTAGATGCAAGATTATTTTGGATGATGAT	1157
Š	264	LysThrLeuglaThrAspSer1leAspSerPheGlaThrGlaAteThranka Thadaer	Ξ.
qq	1158	AAAACTCTTCAGACTGATTCTATAGACAGTTTTGAAACACAGAACACCCACGAAAAAGT	1217
οy	284	AshikeuAspGluGluValAshVallleProProProHisThrProValArqThrValMetAsh	¥0¥
qq	1218	AACCTTGATGAAGGTGAATGTAATTCCTCCACACACTACCAGTTAGGACTGTTATGAAC	1277
ò	304	ThrileGinGinLeuMetMet.IleLeuAsnSerAlaSerAspGinFroSerGiuAsnLeu	171
106	1278	ACT AT CCAACAATTAATGATTTTAAATTCAGCAAGTGATGAAGTTTAGAAAATATGA	1 4 4 7
ć	324	IteSerTyrPheAsaAsaCysThrValAsaFrcLysCluSerIJ eLedgsAt4Vallys	4 4
qq	1338	ATTICCTATITIAACAACTGCACAGTGAATGCAAAAGAAAGTATACTGAAAAGAAAG	1 1497
ογ	344	AspticelyfyrliephetyselutysPheAtatysAtaVatelychelyfesVatetu	¥9.¥
qq	1398	GATATAGGATACATCTTTAAAGAGAAATTTGCTAAAGGTGTGTGT	1457
δλ	364	lleGlySerGlnArqTyrLysLeuGlyValArqLeuTyrTyrAraValMetGluSerMet	£
Q	1458	APTIGGATCACAGCATACAAACTTGGAGTTCGCTTGTATTACCGAGTAATGGAATCCATG	1517
δλ	384	LeuLysSerGluGluGluArgLeuSerIleGluAsnPheSerLysLeuLeuAsnAspAsn	4 0 4
qq	1518	CTTAAATCAGAAGAAGAAGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAAC	15.77
Oy	404	LepheHisMetSerLeatLeatLeatLeatLeatLeatLeatLeatLeatLeat	424
qq	1578	ATTITICATA FGECTITATIGG CGTG CGCTCTTGAGGTTGTAATGGC CACATATAGCAG	16.47
δ	424	SerThrSerGluAsnLeuAspSerGlyThrAspLeuSerPh@ProTrpI]eLeuAsnVal	44.
qu	1638	AGTACATCTCAGAATCTTCATTCTGGAACAGATTTGTCTTTCTCAGATCTCGAATGTG	1697
ς	444	LeuAsnLeuLysAlaPheAspPheTyrLysVallledluSerPhelleLysAladly	46.4
qq	1698	CTTAATTTAAAAGCCTTTGATTTTTACAAAGTGATCGAAAGTTTTTATCAAAGCAGAAAGC	1757
οy	464	AsniculibrardiuMet HebyshistondiuAraCyscluBisArdToMet Cluser	48.5
qo	1758	AACTTGACAAGAGAAATGATAAAACATTTAGAAGGATGTGAAGATGGAATGGAATGC	1817
ζŎ	484	LeuhlaTrpLeuSerAspSerProLeuPheAspLeuTleLyst3LiSerLysAspAratiu	5.03
qci	1818	CTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAAAAAAAA	1877
ò	504	GlvProThrAspHisLeuGluSerAlaCysProLeuAsnLeuProleuGluAsnHis	124

(first entry)

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                                                                         5.4 ThrAlaAlaAspMetTyrLeuSerProValArgSerProLysLysLysGlySerThrThr 543
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stomach; lung; prostate; pancreas; carcinoma; antitumour; cancerous;
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Breast cancer related gene sequence SEQ ID NO:1210.
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Claim 1: SEQ ID 1210; 44pp; English.

adenoratrinoma, carcinoma, clear cell cancer, infiltrating ductal cancer, the present invention describes a method (M1) for serecting for an anti-neoplastic agent. The method involves exposing cells to a chemical agent to be rested for anti-neoplastic activity, determining a change in expression of at least one que (I) of a signature gene set, where (I) comprises a sequence (S) selected from 8447 sequences (qiven in ABL51664 to ABL70110), or is at least 95% identical to (S), where a change in expression is indicative of anti-neoplastic activity. (1) has eyeostatic activity and can be used in one therapy. MI can be used for serecting and out in emphasic agent, and can be used for producing a product, which is the data collected with respect to the anti-neoplastic agent as a result of ML, and the data is sufficient to convey the chemical structure and/or properties of the agent. MI can be used in the treatment of cancer such as colon, breast, stomech, bund, thyroid, wesophageal, ovarian, Figure 1. intilliating lobular cancer, squamous cell carcinoma, neuroendocrine carcinoma, papillary carcinoma and Wilm's tumour. 8×35666666666666666666666668×8×

Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other;

Conservative: Mismatches: Matches: motors: Length: 41.70% 91.708 98.838 Best Local Similarity: Percent Similarity: All-tument Scores:

104 TleSerThrJulleAsnSerAlaLeuValLeuLysValSerTrpHTeffrPhetLeuLeu 123 4 (N. ATCTGTATCTTTATTGTAGGAGTTGAGGTAGATGTCGTTCACTTTACTGAGGTA 497 HELLITTELLIT 618 (TOTTCAGGAAATGGAAAGGACAEGTGAACTTATATATTTGACACAAGCAGGAGTTGG 677 258 GACCTGEOTCTGGTCAGGCTTGAGTTTGAAGAAACAGAAGAGAGAGTGATTTTACTGCATTA 317 4.18 TGTCAGAAAFTAAAGATACAGATGATGTCAGAGAGGAGGGTTGGTTAACTTGGGAGAAA 377 (2) STELCATGLGGAGTALGGGAGTGGGAGGTTALATTCAAAAGAAAAAGGAACTGTGGGGA 437 198 COGNAAAAAAAATAGAAATGAGTGTCGAAAATTGTTTAACTTACTAAAAGAAATTGATAGC 557 ValAspLeuAspGluMetSerPheThrPheThrGluLeu 43 44 GINLYSASRILIGILLIGSETVALHISLYSPherbeAshLeuLysGluffeAspThr 63 64 SetThitysValAspAsuAlaMetSetArqLeuLysLysTyrAspValLeuPheAla 83 1 MethroprobysihrPreArqLySihrAlaAlaThrAlaAlaAlaAlaAlaAlaGluPre 20 #4 LouPheSerLysLeuGluArqThrCysGluLeuIleTyrLeuThrGlnProSerSerSer 21 ProAlaProProProProProProGlu-------US 09 026 459A 39 (1 851) x ABL62873 (1-4839) ouery Match: DB: 5 <u>-</u> <u>.</u> <u>=</u> Ē : -= $\frac{1}{2}$ 3 5 Ξ 5 $\frac{1}{2}$ Ξ Ē ŝ Š

484 LeuAlaTrpLeuSerAspSerProLeuPheAspLeuIleLysGlDSerLysAspAruGlu 504

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038 AATTCTCTTGGACTTGTAACATCTAATGGACTTCAGAAGGTGAAAATTTTTAAACGA 1097 978 CATGAATGTAATATAGATGAGGTGAAAAATGTTTATTTCAAAAATTTTATACTTTTATG 1037 .278 ACTATICAACAATTAATGATGATTTTAAATTTGAGGAAGTGATGAAGGTTGAGGTTGAGAAATGTG 1337 338 ATTICCTATITIAACAACTGCACAGAATCCAAAAGAAAGTATACTGAAAAGGGGAGTGAAG 1458 ATTIGGATCACAGCGATACAAACTTIGGAGTTGGTTTGTATTACCGAGTAATGGAATCCATG 1517 1518 CTTAAATCAGAAGAAGAACGATTATCCAATTCAAAATTTTAGGAAACTTCTGAATGACAAC 1577 1758 AACTIIGACAAGAGAAATGATAAAACATTIAGAANGATGTGAAGATNGAATGATGGAATTO 1817 76.4 ₹23 384 LeutysSerGluGluGluArqLeuSerTleGlnAsnPheSerLysLeuteuAsnAspAsn 403 404 HePheHisMetSerLeuLeuAlaCysAlaLeuGluValValMetAlalmTyrSerArg 423 424 SerThrSerGlnAsnLeuAspSerGlyThrAspLeuSerPheProTrplleLeuAsnVal 443 444 Leuastileutysalapheasppheryrtysvalttegtuserphettetysalagtugty 463 464 AsniculhrargGiuMetileiysHislauGluarqCysGiuHisarqHeMetGluser 483 184 AlaArqIleAlaLysGlnLeuGluAsnAspThrArqIleIleGluVulLeuCysLysGlu 203 144 CysValleuAspTyrPhelleLysLeuSerProProMetLeuLeuLysGluProTyrLys 163 164 ThralaVallleProlleAsnGlySerProArqthrProArqArqGlyGlnAsnArqSer 183 918 GCACGCATACCAAAACAACTAGAAAATGATACAAGAATTALTGAAGTTCTCTGTAAAGAA 977 124 AlaLysGlyGluValLeuGluMetGluAspAspleuVallleSerPheGluLeuMetLeu 143 344 AspiledlyTyrilePhetysGlutysPheAlatysAlaValGlyGlnGlyCysValGlu 224 AshSert.cuGlyt.cuVallhrSerAshClyt.cuProCluValGluAshtcuScrt.gsArg 304 ThrileGinGinLeuMetMetLieLeuAsnSerAlaSerAspGinProSerGluAsnLeu 324 HeSerlyrPheAsnAsnCysthrValAsnProLysGluSerHeLeutysArqValLys 204 Hisotogyaan Praspoluval psastvolyptital parameter in alameter (1914) 244 TyrGluGluIleTyrLeuLysAsnLysAspLeuAspAlaArqLeuTheLeuAspHisAsp 284 AsnLeuAspGluGluValAsnVallleProProHisThrProValArgThrVaiMetAsn 264 LysThrLeuGinThrAspSerTleAspSerPheGluThrGLuArqHhrProArdLysSer 364 IleGlySerGlnArqTyrLysLeuGlyValArqLeuTyrTyrArqValMetGluSerMet 9 a Q C C q a q q 3 qq Š ò 3 ô 9 ं a ð ŝ 3 ò ò 3 ò ò 5 ò ò ò ò ò ò

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3 5.7	i AraValAsuserthrAlaAsnAladiuthrGloAlathrSerAlaPheGloThrGloLys 56 	544 1998	<u>.</u>
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The sequence is that of the DNA sequence encoding a retinoblastoma tumour protein. The generate be used in a movel method involving a recombinant addrewing a xypression vector to treat diseases associated with the ansence of the TSG or the presence of a mutated TSG, e.g. many forms of carcinoma, sickle cell anaemia or Tay-Sach's
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                                                                                                                                 Recombinant, adenovirus, expression vector; TSG; small luna cancer; hepatocarcinoma; melanoma; retinoblastoma; sarcoma; sickle cell; anaemia; Tay-Sach's disease; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            foreign gene - esp. encoding tumour supplessor protein for gene therapy of fumours, reduces contamination by wild type adenomius
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Ademoviral vector with deletion of viral protein IX contains
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Sequence 2995 BP; 975 A; 617 C; 594 G; 809 T; 0 other;
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                                                                                                        Retinoblastoma tumour suppressor gene.
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                           AAQ90059 standard; DNA; 2995 BP.
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93US-0142669.
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4	4.93	ONGANANATAGAAAATGAGGATGAAAATTGTTTAAGTTAGTAAAAGAAATGATAGG	558
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1.76		97.0	97.0	97.0	97.0	46.7	96.3	96.1	94.7	93.5	92.3	988.6	86.3	85.9	85.1	76.3	76.3	76.3	76.3	76.2	: 96	76.2	76.2	76.2	76.1	76.0	25.1	25.0	9. E	9.9		9.9	u.	ī	9.9
3226	3777	3004.4	3224.4	\$224.4	1222.8	3212.6	3212	1194.4	1148.4	3107	3066.2	2945.2	2867.6	2855.6	2827.4	25 44	2534	2534	25 34	2531	2532	2531	25 41	25 41	2529.4	2524.6	8 15	831.8	220.8	220.8	220 8	220.8		x X	218.8
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ALIGNMENTS

AAV58446 standard; DNA; 3323 BP. RESULT 1 AAV58446

AAV58446;

02-DEC-1998 (first entry)

Medified tetihoblastoma tumout suppressor gene.

Modified retinalization times adjectsor; KTSP protein; cancer therapy; cellular proliferation inhibitor; ss.

Homo sapiens.

Location/Qualifiers 7..2562 /*tag= 4 Key

W09837091-A2.

27-AUG-1998.

98WO-US04041 19-FEB-1998;

97US 003B11B

20-FEB-1997;

(BAYU) BAYLOR COLLEGE MEDICINE (TEXA) UNIV TEXAS SYSTEM.

Benedict WF, Hu S, Xu H, Zhou Y;

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                                                                                                                                                                            protein (RISP) of the invention. The proteins can be used for inhibiting eachilds profiler protein. The RISPs can be used for treation, when conditions treated with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular profiferation, particularly cancers. The RISPs have a broader spectrum of
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                                                                                                                                                                                                                                                                                                                                                                                                                                        0; Gaps
                                                                                                                                                       This sequence encodes a modified relinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                     100.0%; Score 3323; DB 19; Length 3323; 100.0%. Pred. No. 0;
                                                       Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                              indels
                                                                                                                                                                                                                                                                                                  Sequence 3323 BP; 1099 A; 647 C; 588 G; 989 T; 0 other;
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                                                                                                                                                                                                                                                                                                                                                                            0; Mismatches
                                                                                                                    22, Fage 180 184, 249pp, English
                                                                                                                                                                                                                                                        activity than wild type RTSPs.
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Matches 323; Conservative
WFI: 1998-480788/41.
                  F FSUR: AAW69470.
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721 AATGITICIAAAGGAIAGGAAGAAAITTATGITAAAAATAAAGAICIAGAIGCAAGAITA 780

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1021 CTGAAAAGAGTGAAGGATATAGGATACATITAAAGAGAAAFTTGGITAAAGGTGTGGA 1080
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781 TTTTTGGATCATGAYAAACTCTTCAGACTGATTCTAFAGACAGTTTTGAAACACAGAGA 840
                                                                                                                  781 TITITGGATCATGATAAAACTCTTCAGACTGATTCTATAGACAGTTTTGAAACAGAGA 840
                                                                                         841 ACACCAGAAAAAGIAAACTIGATGAAGGIGAAIGIAA11GCIGCAGACACACAGI1 900
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			IGTAACAGCATACAAGGATOTTO TELLITITITITITITITI IGTAACAGCATACAAGGATGTTO	CAAAGAGGGGTATGATTCTA 	BAAAACAAATATTTTGCAGTATG 	CALLOCTORANDOCTTACAAGI IVIIIIIIIIIIIIIIIIIII CATTOCTORAAGOCCTTACAAGI	CTATATTTCACCCTGAAGAGTC 	AATGACTCCAAGATCAACAATCT { }	SFICCAGAAATAAATCAGA FGG FFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	AGGAAGCAACCTAAAACAC TELLITITITITITITITITITITITI AGGAAGCACCTCAAAAAAAAAAAAAAAAAAAAAAAAAAA	NGCAGATGGAAGTAAACATGTCC 	GACTICIACIOGAACACGAATGC HITTIIIIIIIIIIIIIIIII GACTTCIACTCGAACACGAATGC	CAAGGAAGAAATGAGGATCTC 	TGTCTCTCACAGAIGTGACTGT 	ATCTTCACCTCTCTCTCTCTCCATA 	GCCACTTGAAATGTTAGTCATTG	SCATTTAAAAAGTTGTAGCAGAT 	SATAGTAAGAATGGCCCTAGAGT HILLILLILLILLITITITI SATAGTAAGAATGGCCCTAGAGT	CCTCTTTTGTAGCATATAGGTG 	[[]]]]AATTTAACATGAACACCC
			ATAGACCTTAAALICAAAALGAL TITTITITITITITITITI ATAGACCTTAAATTCAAAATGAT	GAGACALICAAACSIGIILIGALGALGALGALGALGALGALGALGALGALGALGALGALG	AACTOGGTCTTCATGCAGAGACTC FELLITITITITITITITITITITI AACTOGGTCTTCATGCAGAGACTC	POTAGOTTOTOACTAATAOCTOA TITUTTITITITITITITITITITI COTAGOTTOTOACGAATAGOTOA	TTACGGATTCCTGGAGGGAACATC FFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	GAAGGTCTGCCAACACCAACAAA 	GAATCALICOCGACTICIGAGAACIIIIIIIIIIIIIIIIIIIIIIIIII	CGTGTGCTCAAAAGAAGTGCTGA FEEFFEEFFEEFFEEFFEEFFEEFFEEFFEEFGAAAAGAAGTGGCTCAAAAGAAGTGCTGAAAAGAAGTGCTGAA	TITGATATTGAAGGATCAGATGA HHIHHHHHHHHH TITGATATTGAAGGATCAGATGA	TTTCAGAGAAACTGGCAGAATG HTTTTAGGAGAAACTGGCAGAAATG TTTCAGGAGAAACTGGCAGAAATG	AATGATAGPATGGATACCTCAAAC TITTITITITITITITITITI AATGATAGCATGGATACCTCAAAC	CASTGTGTACACCTCTGCATTCACTTCACTTCACTTCACT	TTP GPTTA POCCCACA FTTAATI HTTT FTTT FTTT FTTT FTTT TAATI	OCANITGITTGGGTGATTGGTAAC 	TTGAAAATCTTGTGTAAATCCTG TTGTGTGTGTGTGTGTGTG TGAAAAACTTGTGTAAATCCTG	AAGTAAAATTOOTGEOTTTATG TITTITTTTTTTTTTTTTTTTTTTTTTTTTTTT	COCAGGOTOTOTGACTACTTTG FEETHELLIELLELOTTE POPAGGOTOTOTGACLACTTG	HIIAIIAAHIIAFALGIAIATI

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protein (KISP) of the invention. The proteins can be used for inhibiting celular proliferation, when coadministered with a p54 protein. The KISPS can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The KISPs have a broader spectrum of activity than wild type KISPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Modified retinoblastoma fumour suppressor; RTSP protein; cancer therapy;
                                                                                                                                                     3180
                                             3181 TAATTAAATAAAAGCTGGAAGCAAAGTATAAGCATATGATACTATGATACTAGTAGTAGTAATAAAAAA 3240
                                                                                                                                                                                                                                                                       224. GATTTCATACCTCAGAATGTAAAAGAACTTACTGATTATTTTCATCATCAAACTTATGTT 3400
                                                                                                                                                                                                                                                                                     2941 TGTTTTATTATTATTATATGTATTTTTTTAATTTAACATGAACACCTTAGAAAATGT 8000
                             3001 GTGGTATCTATCTAAAAGCAATITGATIGAGTGGCCATTGACTAAAATTATCTGAA 3060
                                                                                      3121 GATTITATITIACTATIGGAALCIGAIASACTGIGIGGITGIIITALAAAATIIIGATTI
                                                                                                                                                                                                                              This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Retinoblastoma suppressor protein with N terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Modified retinoblastoma tumour suppressor gene.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             cellular proliferation inhibitor; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Location/Qualitiers
7..2700
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                                                                                                                                                                                                                                                                                                                                 3301 TTTAAATGAGGATTATTGATAGI 3323
                                                                                                                                                                                                                                                                                                                                                              3301 TITAAATGAGGAITATTGATAGT 3424
                                                                                                                                                                                                                                                                                                                                                                                                                                        AAV58447 standard; DNA; 4461 BP.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  02-DEC-1998 (first entry)
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 (TEXA ) UNIV TEXAS SYSTEM
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Homo sapiens,
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	Gaps	155 293	215 353	275	335 473	395 533	455 593	515 653	575 713	635 773	695 833	755 893	815 953	875 1013	935	995 1133	1055	1115
Sequence 3461 BP; 1141 A; 675 C; 627 G; 1018 T; 0 other;	overty Match 97.1%; Score 3228; DB 19; Length 3461; Best Local Similarity 100.0%; Pred. No. 0; Matches 3228; Conscrative 0; Mismatches 0; Indels 0; G	95. GGTPGAPCTAGATGAGATGTCGTTCACTTTTACTGAGCTACAGAAAAACATAGAAATCAG TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	156 IGECCATAAATETETTTAACTTACTAAAAGAAATTGATACCAGTACCAAGAGTTGATAATGC 	216 TATGECAAGACEGEGAAGAAGEATGATGGETGGCACECTTCAGCAATTGGAAGGAAGGAAGGAAGAGAAGA	275 GACATGIGAACHIAIATATITGACACAGCCAGCAGCAGTTCGATATCTACTGAAATTACTTCACTGAAATTACTTCACTGAAATTCACTGAAATTCACTGAAATTCACAGCAGTTCGATATCTACTGAAATTCACAACCAGCAGTTCGATATCTACAAAATTCACAAAATTCACAAAATTCACAAAATTCACAAAATTCACAAAATTCACAAAAATTCACAAAAATTCACAAAAATTCACAAAAATTCACAAAAATTCACAAAAATTCACAAAAATTCACAAAAATTCACAAAAAA	4.6- ISDALIOGIGGIAGAAAGTTTTT GGALGAGATTTTTTATTAGTAAAGGGGAGTATTAGA 	 AATGGAAGATGATGGAGATTTCATTTCAGTAADGCTATGTGTGCTTGACTATTTAT IIIIIIIIIIIIIIIIIIIIIIIII AATGGAAGATGACTGATTTCATTTCAGTTAATGCTATGTGTGTG	456 JAAACTGTCACCTCCCATGTTGCTCAAAGAACCATATAAAACAGCTGTTATACCCATTAA 	515-10011CACPT-CGAACACCCAAGCGAGGTCAGAACAGGAGTGCACATAGCAAAAAACT TITTITITITITITITITITITITITITITITITITI	6. AGAAAATGATACAAGAATTATTGAAGTTCTCTGTAAAGAACATGAATGTAATATAGATGA (111111111111111111111111111111111111	6.46 GGIGAAAARGITTATTTCAAAATTTTAYACCTTTTATGAATTCTCTTGGACTTGTAAC 	696 ATCTAATGGACTTCCAGAGGTTGAAATCTTTTCTAAACGATACGAAGAAATTTATCTTTAA 	755 AAATAAAGATCTAGATGCAAGATATTTTTGGATGATGATGAAAAGTGT GCAGAGTGT GAATTG GAGGAGGAGGAGGAGGAGGAGGAGGAAGAGGAGGAAGAGGAGGAGGAGGATATTTTGGATGAT	8.5. TATADAGASTITIGAARGAGAGAGGAGGAGAAAAGTAACCTTGATGAAGAGGGAAA TELLITITITITITITITITITITITITITITITITITIT	*75 TOTAATTOOLOCACACTOCAGTTAGGACTGTTATGAACACTATGCAACAATTAATGAT FELFELFILLELLELLELLELLELLELLELLELLELLELLELLELLE	936 GATITIAAATICAGCAAGTGATCAACCITCAGAAAATCIGATTTCCIATITAACAAACTG 31 THILLIHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	996. CACAGIGAA ICCAAAAGAAAGTATACIGAAAAGAGGGAAGGATATAGGATACATCTTTAA 	95. AGAGAAATITGCTAAAGCTGTGGGAÇAGGGTGTGFCAAAATIGGATCACAGGGATACAA TITTITTTTTTTTTTTTTTTTTTTTTTTTTTTT
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2075 1176 ATTATCCATTCAAAATTTTTGCAAACTTCTGAATGACAACATTTTTCATATGTCTTTALL 1235 1236 GGCGCGCGCGCTCCTGGGGTTCCTAALGGCCACAAAATAAGAAAATACACATCTCAGAATCTTGA 1295 1434 TTCTGGAACAGATTTGTCTTTCCCATGGATTCTGAATGTGCTTAATTTAAAAGCCTTTGA 1493 1476 ACCITINITIGALCITATIAAACAAFAAAAAAAAAAAAGAGGAACTGATGATCACCTTGA 1535 1536 ATCTGCFTGTCCTCTTAATCTTCCTCCAGAATAATCACACTGCAGCAGATATGTATCT 1595 1734 TTCTCCCGTAAGATCTCCAAAGAAAAAAGCTTCAAGCGTGTGTAAATTCTAGTGAAA 1793 1656 IGPAGAGAPANAMACICAGCCITCCAGACCAGAAGCATGAAATCTACCICT 1715 1854 ITCACIGITITALAAAAAAGIGTAIGGGGTAGGGTAGGGTAGGGGTAAAIACACIIIGIGA 1913 1836 CTTGCAGAATGAATAAGAACTCATGAGAACAAGCAIIGGACCAAATTATGATGTGTC 1895 1956 AIACAAGGAICTICCICAIGCIGIICAGGAGACAIICAAAGGIGITITGAICAAAGAAGA 2015 2214 TATTITIGASTATSCITCCACCAGSCCCCCIACITGTCACATACCICCACAGACCCC 2273 1194 AGAGAAFFFGFFAAAGFFGFGAAAAGFFFFFFFFFFAAAAFFFGGAFFGGAFFGGAFFGGAFF 1116 ACTIGGAGIIGGIIGIAIIAGGGAGIAAIGGAAICCAIGGIIAAAICAGAAGAAGAAGG 1374 GGCCHOCCCCCTCCACCTTCTATGGCCACATAIGGAGAGTACACCTCAGAATGTIGA 1433 1416 AAAACATTTAGAACGAIGIGAACAICGAAICAIGGAAICCCITGCAIGGCICCCAGAIIC 1475 1674 Archectedtetetaarentetetetetaarrakareaengengeagatatet 1733 1596 TICTCCTGTAAGATCTCCAAAGAAAAAGITCAACIACGCGTGTAAAITCTACTGCAAA 1655 1716 PPCACPGPTTTTATAAAAAAGTGTTATGGGTTAGGGTTATGGGGTTAAATAGAGTTTGTGA 1775 1896 CATGTATGGCATATGCAAAGTGAAGAATATAGACCTTAAATTCAAAATCATTGTAACAG 1955 1776 ACGCCTTCTGTCTGAGCACCCAGAATTAGAACATATCATCTGGACCCTTTTCCAGCACAC 2154 SCACTATGALP TAFFAIAIATICIATAACTOSTCIICATGCAGAGTGAAAAAAA 1296 ITCTGGAACAGATTTGTCTTTCCATGGAITCTGAAIGTGCTTAATTTAAAAGCCTTTGA 2034 CATGTATGGTATATGTAAAGTGAAGAATATAGAGCTTAAATLGAAAALCATTGTAACAGC 2076 TATITTGGAGTAFGGTTFGGAGGGGGGGGGTTGFGGGAATAGGTGAGATAGGGAIFGG ġQ. qq qq qq Dp q ò CP Š Ω ò Ś ΩY ò ò qq 9 ò g 급 ò ò

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6054 GTACCATAFAGGLGATGLITTOGTTTTTTTATTAATTTATGTATTTTTTTATTTT 3113
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                                                                                                                                                                                2436 ANGTANACATCTCCCAGGAGACTCCAAATTTCAGCAGAAAACTGGGAAAAATGACTTCTAC 2495
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           2676 TOTH FERIOGA FALAAAA FORGOLAGA FORAATTI GETTTGGGTGATTECT AAGCCACTTGA 2735
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        AAGTTGTAGCAGATTGTTTCCTTCCAAAGTAAAATTGCTGTGTTTATGGATAGTAAG 2855
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              4174 GCCCATTCACCAAAATTATGCTGAAGTGTTGTGGAAAAATGGATATTATTAGAAATTAGA 3233
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                                                                                                                                                             2315 AATAAATCAGATGOTALGTAACAGGGACCGTGTCAAAAGAAGTGCTGAAGGAAGCAA 2375
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2196 ACCOTGAAGAS FOGATATAAAATTTCAGAAGGTOTGGCAACAAAAATGACTGC
                                                                                                                    2.994 AAGATCAAGAATCTTAGTATCAATTGGTGAATCATTCGGGACTTCTGAGAAGTTCCAGAA
                                                                                                                                                                                                                                                                    26.44 TCGAACACGAATGCAAAAGCAGAAATGAATGATAGCATGGATACCTCAAACAAGGAAGA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           2616 ACAGATGTGACTGTATAACTTTCCCAAGGTCTGTTTATGGCCACATTTAATATCTTCAGC
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This sequence encodes a modified retinoblastoma tumour suppressor protein (RTRP) of the invertion. The protein can be used for inhibiting cellular proliferation, when coadministered with a psy protein. The RTSPs can be used for treating diseases characterised by abnormal cellular.
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                                                                                                                                                                                                                                      Modified retinoblastoma tumour suppressor; RISP protein; cancer therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               270 GGAAAGGACATGTGAACTTATATATTTGACACAACCAGCAGTTCGATATCTACTGAAAT 429
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            90 TCCTGAGGTCGACCTAGATGAGATGTGGTTCACTTTTACTGAGCTACAGAAAAAATAGA 149
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Caps
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               150 AATCAGIGICCATAAATICIITAACIIAAAAGAAAIIGAIACOGIAAAAAAIIGA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             210 TAATGCTATGTCAAGACTGTTGAAGAAGTATGATTGTTTTGCACTCTTCAGCAAATT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             97.18; Score 8226; EB 19; Length 4266; 99.88; Pred. No. 0; tive 0; Mismatches 5; Indels 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Retinoblastoma suppressor protein with Neterminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               3414 TTATTTTCTTCATCCAACTTATGTTTTTAAATGACGALTATTGATAGT 4421
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Sequence 3266 BP; 1092 A; 602 C; 574 G; 998 1; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          inhibiting cellular proliteration, particularly cancer
3276 TIAITITCITCAICCAACTIAIGITITIAAATGAGGAITAITGAIAGI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Modified retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Claim 22; Page 166-170; 249pp; English.
                                                                                                                                                                                                                                                      cellular proliteration inhibitor; ss.
                                                                                                                                                                                                                                                                                                                      Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               (MAYU ) BAYLOR COLLEGE MEDICINE.
(TEXA ) UNIV TEXAS SYSTEM.
                                                                                                           AAV58444 standard; DNA; 3266 BP
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      activity than wild type RISPs.
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                                                                                                                                           AAV58444;
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389	392	509	569 512	629 572	689 632	749 692	809	869 812	424 872	989	1049	1109 1052		1229			14095
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1410 AATGATAAAAGATITAGAAGGAGTGBAAGGBAAGATGAGGAAIGCCTIGGATGGCTIGGA 1469 1353 AATGATAAAAGATTTAGAAGGATGTGAATGGAATGGGAATGCCTTGCATGGCTCTC 1412 1473 CCTTGAATCTGCTTCTCTCTTTAATCTTCTCTCTCTCTCAATAATCACACTGCAGGAGATAT 1532 1533 GTATICHTTHOUGTIGTAAGATCTCCAAAGAAAAAGGTTCAAGTAGGGGTGTAAATICTAU 1552 2012 2189 1413 AGAITCACCITIAITIGAICITAITAAACAAICAAAGGACCGAGAAGGACCAACTGAICA 1472 1890 GTGTTTGATGTATATGGAAAGTGAAAGAAATATAGACGTTAAATTGAAAATGATTGT 1949 2430 AGATGGAAGTAAAGATGTGGGAGGAGGGAAATTTGAGGAAAGTGGGAAAALGAG 2489 2250 GACHTCCAAGATGAAGAATGTTAGTATGAATTGGTGAATCATTGGGGACTTCTGAGAAGTT 2309 1590 GTATCTTTCTCTGTAAGATGTGGAAAGAAAAAAAAGGGGTGTGAATTGTAC 1650 TGGAAATGCAGAAGAAGGAAGGTAGGAGGGTTGCAGAGGGGAGAGGCATTGAAATGTAG 1770 TIGIGAAMGMITMIGIMIGAGAGAGAGAATIAGAAMINIAAANIAGAAGAGAGAGAGAGA 1713 TTTCTCCAACCCTTCTCTCTCTCTCACCACCCAGCACTTAGAACATATCAATCTCCACCCTTTTCCA 1893 AACAGCATACAAGGATCTTCCTCTTGTTCAGGAGGATTTCAAAGGTGTTTTGATCAA 1953 AGAAGAGGAGTATGATTGTATTATAGTATTGTATAACTGGGTGTTGATGCAGAGAGTGAA 2130 TOTOGRAMSON STRANDAGITHOSTASTINAS OFTANISATINOTISSAGGRANDIA 2073 TCCFCGAAGCCFTACAAGTTFCCTAGTTCACCTTACGGATTCCTGGAGGAAGTATA 2190 TATITICACCCTGAAGAGTCCATATAAAATTTCAGAAGGTCTGCCAACAACAAAAAT 2253 CCACAAAAYAAATCAGATGGTATGTAACAGCGAGGGTGTGAAAAGAAGTGCTGAAAG 2370 AAGCAACCTTCTTAAACCACTGAAAAACTAGGCTTTGATATTGAAGGATGAGATGAAAC 1530 CCTTGAATCTGCTTTGTCCTCTTAATCTTGCTGCGGGAATAATCACACTGCAGGAGATAT 1710 CTCTCTTTCACTGTTTTATAAAAAGTGTATCGGCTAGCCTATCTCCGGCTAAATACACT 1950 AACAGCATACAAGGATCTTCTTCATGCTGTGTGAAGAAAAATGAAAGGTGTTTGATGAA 2010 AGAAGAGGAGTATGATTGTATTATAGTATTGTATAAGTGGGTGTTGATGCAGAGAGTGAA 2070 AACAAATATTTTGCAGTATGCTTTCCACCAGGCCCCTAGCTTGTCACCAATACCAAA 2193 GAPTPORAGATPARGARPTTRGTATPGATTCGTCAAFCATTCGCGGACTTGTCACAAGTT Ġ. Qγ qq 9 ò qq g <u>1</u> q $\frac{q}{c}$ q **q**0 q q q ò Qγ ò οy $^{\circ}$ δ οy $^{\circ}$ ò

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Modified retinoblasfoma fumour suppressor; RISP profein; cancer therapy;
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4270 TACTGATTATITICTICALCCAAGITATGITITIAAAIGAGGATTATTGATAGT 3323
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This sequence encodes a modified retinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p54 protein. The RTSPs can be used tor treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RTSPs have a broader spectrum of activity than wild type RTSPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        90 TCCTGAGGTCGACCTAGATGAGATGTCGTTCATTTTTACTGAGGTAGAGAAAAAATATAGA 149
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       97.1%; Score 4226; DB 19; Length 4424; 99.8%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Sequence 3323 BP; 1114 A; 605 C; 591 G; 1014 1; 0 other;
                                                                                                                                                                                                                                                                                                                             inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                            Claim 22, Page 158 162, 249pp, English.
                                                                                                                                                                  (BAYU ) BAYLOR COLLEGE MEDICINE
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Modified retinoblastoma fumour suppressor: RTSP profein; cancer therapy; religiar proliferation inhibitor; ss.
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                                 protein (RTSP) of the invention, the proteins can be used to inhibiting cellular proliferation, when coadministered with a p54 protein. The RISPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RTSPs.
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                    This sequence encodes a modified retinoblastoma funtour suppressor
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2259 TAITICACCTGAAGAGTCCATATAAAAIILGAGAAGGTCIGCCAACAACAAA 2318 2379 CCAGAAAATCAGATGGTATGTAAYAGCGAGTGTGTGTGTGAAAAGAAGTGCTGAAAGG 2438 2619 GGAAGAGAAAATGAGGATOTGAGAAOCTTGATGGACAOTGTGTAGACTCTGGATTGATTG 2678 2130 ICCICGAAGCCCTIACAAGIIICCTAGIICACCTIACGGAIICCTGGAGGGAACAICTA 2189 2319 GACTCCAAGATCAAGAATCTTAGTATCAATTGGTGAATCATTCGGGGACTTCTCAGAAGTT 2378 2370 AAGGAACCCTCCTAAAACCACTGAAAAAACTACGCTTTGATATTGAAGGATCAGATGAAGC 2429 2499 AGAIGGAAGTAAANTIGIGGAGGAGGAGIGCAAATIICAGCAGAAANTIGGCAGAAATIGAC 2610 TOTOTOAGAGATGTGAGTGTATAAGTTTGGGAGGTTGTGTTTATGGGGGAGATTFAATATG 2669 2730 ACTIGAAATGITAGICATIGITATITATACAAAATTGAAAATCITGITAATGGIGGGA 2789 3150 ACTIGITOTOTOTOTOTOTOTATAAAATTITTGGTTTTAATTAAAAAGCTGCAAGCAAGTAT 3209 2070 AAGAAATATPPPGGAGTAFGGTPFCAAGGGGGGGGTAAGGFFGTGAAAFAGGFGAAFT 2129 3090 ATTAGAAAAAAATTACTAATTTTACACATTAGATTTTATTTTACTATTGGAATCTGAIAT 4149 2139 AACAAATATTTGCASIAFGCITCCACCAGGGCCCCIACCIGICACCAATACCTCACAT 2559 THCFRACHCGAACAACGAAAAGGAGAAAATGAATGCAATGGATGGATACCTGAAACAA. 2679 TOTOTCAPAGATGTGAPTGTATAACITIONAGGTICTGTTTATGGGGACATTTAATATC 2199 JOCIQGAAGOOTTAAAAGTTTAGIIQAQQOIIAQGGAIIQOIQGAGGGAAGAYGTA 2439 AAGCAACCTCCTAAAAACCACTCAAAAAAACTACGCTTTGAIATTGAAGGAICAGAIGAAGC 2430 AGAMGGAASTAAAGATOMOOGAGAGTOGAATTTOAGGAGAAATTOGGGAGAAADGAG 2250 GACTIGCAAGATIGAAGAATGITAGTATGAATIGGIGAALGALIGGGGGGIIGTGAGAAGTI 2670 ITCAGCICITITICIGGAIAIAAAAIGIGCAGATGCAATIGIITGGGIGATICCIAAGCC 2979 ICITITATACATATAGGIGATGITIGCICITGITITITATIAATITATATATTIT 3030 TIGACTGCCCATTCACCAAAATTATCCTGAACTCTTGCAAAAATGGATATTATTAGAA 2190 TATTTCACCCTGAAGAGTCGAIAIAAAAIIICAGAAGGIGIGGGCAACAGAAAAI AGTAAGAATGGGTAAGAGTGGGAAGTCCTGAAAAACCCTGTCGTGTCTGACTACTTTGGCC 2970 TTAATTTTAACATGAAGACGCTTAGAAAATGTGTCTATCTTATGTTGCAAATGCAATTGA 2850 ò, qq. **q**0 qq qq qq ò ò ď à ò d: ò q OYΩ qq ò QQ $^{\circ}$ $\stackrel{>}{\circ}$ qq ò qq ò ò a ò

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                                                                                                                                                                                                                                                                                                                                  Modified retinoblastoma fumour suppressor; RTSP profein; cancer therapy;
1279 AACCATALGALACTALGALACTGAAACAGATITGALAGGAATGTAAAAGAACT 3338
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                                                                                                     1270 TACHGALIALIIIGIIGALGGAAGIIAIGIIITTAAAIGAGGATTAITGAIAGT 3323
                                                                                                                     Retinoblastoma suppressor profein with N terminal modification
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                              2430 AGATIGGAAGTAAAAATGTGTGTGAGGAGAGTGCAAAATTTGAGGAGAAAACTGGCAGAAATGAC 2489
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Modified retinoblastoma fumour suppressor; RISP protein; cancer therapy;
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99.8%; Pred. No. 0,
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                 cellular proliteration inhibitor; ss.
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WHI: PURH 480796741.

YE WIL: PURH 480796741.

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New retracycline responsive expression vectors - used for the lightly controlled expression of qenes, such as tumour suppressor.

YE Inhily controlled expression of qenes, such as tumour suppressor.

YE Inhily controlled expression of qenes, such as tumour suppressor.

YE Disclosure: Pages 145-150; 190pp; Endlish.

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                                                                                              THE HE STRITTERATETATEGENIATECANASTGAAGATATAGACCTTANATTCANAATCATTGT 1949
                                                                                                                    21.21 GTG110CA1G1ATGGGAAGTGAAAGTGAAGAGAATATAGACCTTAAAATTGAAAATGT 2180
                                                                                                                                                                                                                                                                                                        2000 AACAAATAITTTGGAGTAGGTGGAGGTGGGTGGTGGTGAGGAGGAGTAGGTAT 2129
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                                                                                                                                                                                                                                                                                   24.21 TATTTCACCCCTGAAGAGTCCATATAAATTTTCAGAAGGTCTGCCAACACCCAACAAAAAT 2480
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                    2130 TCCTCGAAAGCCTIACAAGTTTCCTAGTTAACTTAAGGAITCCTGGAGGAACATCTA
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hEST2: Lelomorase; catalytic subunit; reverse transcriptase; life-span; retinoblastoma; p53; tumour suppressor; inhibitor; arteriosclerosis; proliferation, immortal, tumour therapy; macular degeneration; activator;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       The invention concerns methods and reagents for extending the life-span, a gill the number of miteria divisions, of a cell. The method relies on activation of a telomerase activity and inhibition of one or both of a refinehlastems (PP)/TIMA palhway or a p53 palhway Phospherylation of Rb by cyclin-dependent kinases, cdk4 and cdk6, releases the cells into the division cycle. Binding of iNK4 family members, e.g. the tumour
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            comprises administering agents reversibly activating telemerase activity and reversibly inactivating RECTARA and/or p53 pathways weeful
3141 **CTTTTTGTAGCATATAGGTGATGTTTGCTCTTGTTTTTATTAATTTATATGTALATTT11 3200
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          New method for increasing the proliferative capacity of cell lines
                                                        2976 ITAAIITAAGATGAAGAGGGIIAGAAAAIGIGIGGIALGIAIGITGGAAATGGAATITGA
                                                                                              3201 TTAATTTVAACATGAACACCCTTAGAAAATGTGTCCTATGTATGTTCCAAATGCAATTTGA
                                                                                                                                                                                                               3030 TTGACTGCCCATTCACCAAAATTATCCTGAACTCTTCTGCAAAAATGGATATLALTAGAA
                                                                                                                                                                         3261 TTGACTGCCCATTACTCCTATACTCTGAACTCTTGCAAAAATGGATATTATTAGAA
                                                                                                                                                                                                                                                   3150 ACTGTGTGTTTTATAAATTTTGCTTTTAAAIAAAAGCTGGAAGCAAAGTAI
                                                                                                                                                                                                                                                                                                                              3210 AACCATATGATACTATCATACTGAAACAGATTTCATACCTCAGAATGTAAAAGAACT
                                                                                                                                                                                                                                                                                                                                                                                                                                           3270 TACTGATTATTTTCTTCATCCAACTTATGTTTTTAAATGAGGATTATTGT 3323
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 3501 TACTGATTATTTTCTTCATCCAACTTATGTTTTTAAATGAGGATTATTGATAGT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Claim 5; Page 121-123; 123pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               in treating age related diseases
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                30
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              AAA29391 Standard; DNA; 4839
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      L2-SEP-2000 (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Human retinoblastoma gene.
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suppressor plankeds, inhibits kinase activity and results in growth an arrist. But hactivates an selectively and recensibly hactivate and the CNM4 pathway repertings as selectively and recensibly hactivation and the pS3 tumour suppressor is a cellular inhibitor of Rb/R2F function and the pS3 tumour suppressor and ear also be used in the methods, other molecules which can be used in include odds or odds mutatis. In particular, a cdk4 mutant is one which additional constructs include a papilloma virus B7 protein, or other viral ouroproblem which bypasses Rb and/or pS3. Antisense constructs of the Rb and planked actual bypasses Rb and/or pS3. Antisense constructs of increasing the proliferative expantly of cells. The cells are useful for increasing the proliferative expantited and cosmictly preparations used to treat conditions related to (premature) against e.g. macular degeneration and afteriorsis. The cells are useful for and arterioselerosis. The cells and physicological aspects of these in vitro and for studies on biochemical and physicological aspects of use in the production of normal or quentically engineered.

Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 1; 0 other;

. O 992 AGA IGAGGI GAAAAATGITIAI IITGAAAAI IITIA I AGGITITA IGAAI I GITIAGGAGT 690 EGTAACATOTAALGGACTI COAGAGGTI GAAAATGTI FOTAAACGA FAGAAGAACTITTA 749 450 TITTATT AAACTOLOACCLOTO FIGTTGOTCAAGAAGGATATAAAAGAGCTGTTATAGC 509 510 PATTAATGITTPACCTGGAAPAPPAGGGGGGGTGAGAAGAGGAGGAGGAGAA 569 570 ACAACTAGAAAATGATACAAGAATTATTGAAGTTCTCTGTAAAGAACATGAATGTAATAT 629 932 ACARCHAGAAAATGATGAAGAATFGTFGAAGTTCTCTGTAAAGAAGATGAATGTAATAT 991 6.89 AGATGAGGICAAAAAFISTSTALTICAAAAATTITTATAGCTTTTTATGAATTGTGTTGGGCT 689 250 TCTTAAAAATAAAGATCTAGATGCAAGATTATTITTGGATGATGATAAAAACHCTTCAGGC 809 90 TOTICAGGLOGACO FACALGAGA FOLOGINGACITTI ACTGAGCIACAGAAAAAAAAAA 149 150 AATGAGTGTGCATAAATTGTTTAAPTTAGTAAAAGAAATTGATAGCAGTACGAAAGTTGA 209 210 TAATGCTATGTACAGAGTGTTGAAGAAGAAGTATGTATTGTTTGGAGTGTTGAGGAAATT 269 270 OGAAAGGACAIGIGAACIFAIAIFIGACACACCAGCAGFFCGAIAFCIACFGAAAT 329 692 AAATTCTGCATTGCTGCTAAAAGTTTCTTGGATCACATTTTTTAGTTAAGGGGAAGT 751 990 ATTACAAATGSAASATGATCTGGTGATTTCATTTCAGTTAATGGTATGTGTCGTTGACTA 449 HITTATTAAACTGTCACGTCCCATGTTGCTCAAAGAACCATATAAAAAGGTGTTATAACC 512 AATGAGTGGGATAAALICLITAACITAGAAAAAAAATTGATAGGAGAGAAAGTTGA 571 Caps : () ouery Match 97.1%; Score 3226; DB 21; Length 4839; Best Local Similarity 99.8%; Pred. No. 0; Indels ., 0; Mismatches Matches 3229; Conservative 5 = ... ŝ 5 3 Ē ŝ 5

	810 IGATICIALAGAGILLIGAAAYAQAGAGAGAAAAGIAAGILGALGAAGA 869
GGTGAATG1 GTGAATG1	AATTOCTCCAPACACTCCAGTTAGGACTGTTATGAACACTATCCAACAATT 929
AATGATGAI AATGATGAI	ITTAAATICAAGAAGIGAICAACTICAGAAAATGIGATTICCTATITTAA 989
CAACTGCACATTTTTTTTTTTTTTTTTTTTTTTTTTTTT	AGTGAATCCAAAAGAAAGTATACTGAAAAGAGTGAAGGATALAGGALACAT 1049
CTTTAAAGAC	AAATTIGGTAAAGGIGIGGGACAGGGITGIGIGGAAATTGGAICACAGGG 1109
	HIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII
ATACAAACT1 ATACAAACT1	IGGAGTECGCTGTATTACCGAGTAATGGAATCCATGCTTAAATCAGAAGA 1169
AGAACGATTA	HCCAFTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTTCAFATGT 1229
TTTATTGGGG	IGGGGCTGTGAGGTTGTAAFGGCAVATATAVGAGAAGTAVATATATAAA 1289
TCTTGATTCT	GGAACAGATTIGTCTTCCCATGGATTCTCAATGTGCTTAATTTAAAAGC 1349
CTTTGATTTT	FACAAAGIGAIGGAAAGITTTALGAAAGAGAAGAGAACHGAAAGAGA 1409
AATGATAAAA	CATTIAGAACGATGIGAACATCGAATCATGAAACCCTTGATGACTGCTTC 1469
AGATICACCI	TTATTIGATCITATTAAACAALCAAAGGACCGAGAAGGACCAACTGATCA 152º
CCTTGAATCT	SCTIGICCI CITAALCI ICCI CI CAJAA IAA I CACACHO ACACAGA IAT I 15E
	ELI IIII ELI IIIII IIIIIIIIIIII ELI ELI
GTATCTTTCT	CCTGTAAGAICTCCAAAGAAAAAAGITCAACTACGCGTGTAAATTCTAC 164
	FILLELLELLELLELLELLELLELLELLELLELLELLELLE
TGCAAATGCA TGCAAATGCA	GAGACACAAGCAACCTCAGCTTGCAGACCAGAAGCCATTGAAATCTAC 126 FELLITELLITELLITELTTELTTELTTELTTELTTELTTE
CTCTCTTTCA	CEGETETEARAAAAAGEGRATCEACTAGCCIATCEGGCTAAAIACACT 176
	ELLITELETETETETETETETETETETETETETETETETE
TTGTGAACGG	CCTICTOTCTGAGCACCAGAATTAGAACATATCATCTGGAACCTTTTCCA 1829
	ELLELELLELLELLELLELLELLELLELLELLELLELLE
GCACACCCT	IGAGAATGAGTAFGAACFCATGAGAGAAGATTTGGAAGAATTATGAT 1889
GTGTTCCATGT,	HATGGCALATGCAAAGTGAAGAATALAGACCTTAAATTCAAAALCALTGE 1949

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2810 AGAAGAGGAGTATGATTGTATTATAGTATTGTATAGTTGGGTGTTGATGCAGAGAGTGAA 2069
                                                                                                                                                                                                                                                               2070 AACAAATAFITTGCAGTATGCTTCCACCAGGCCCCCTACCTTGTCACAATACCTCAGAT 2129
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                                                                                                                                                                                                                                                                                                                                                                                  24.42 FECT GRANGE CLIACANG TTI CETAGLI CACCETTA CGATICCT GAGGAACATETA 2551
                                                                                                                                                                                                                                                                                                                                                                                                                                                        2190 TATTTCACCCTTGAAGAGTCCATATAAAATTTCAGAAGGTCTGCCAACACAAAAAT 2249
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                      22% GIGITICCATGLATGCCAFATGCAAAGTGAAGATATAGACCTTAAATTCAAAATCATTGT 2311
                                                                   1950 AACAGCATACAAGGATCTTCCTCATGCTGIICAGGAGACATICAAACGTGTTTTGATCAA 2009
                                                                                                                   2.3.12. AACAGCA1ACAAGGATCTFCCTCATGCTGTFCAGGAGACATTCAAACGTGFFFTGATCAA 2371
                                                                                                                                                                                                               25%2 IATITCACCOCTGAAGAGTCCATATAAAATTTCAGAAGGTCTGCCAACAACAAAAAAT 2611
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       2619 PTGTGAGAGATGTGAGTGTATAAGTFTGGGAGGTTGTGTTTATGGGGGAGATTTAATATG 2669
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The present sequence encodes a human androgen receptor coactivator designated Rb. Androgen receptor co-activator proteins from the present invention can be used in screening assays to identify condidate pharmaceutical molecules for the ability to promote or inhibit the interaction of androgen receptors and androgen responsive elements to modulate androgen activity. The identification and characterisation of androgen co-activity such as those of the invention will
3332 TTAATTTAACATGAACACCCTTAGAAAATGTGTCCTATCTAICTTCCAAATGCAAHT1GA 3391
                                3030 TIGATGATATTATGAAAATTAIGGIGAAGIGIIGIGGAAAAATGGAIATTATTAGAA 3089
                                                                     3392 IIGACIGECEATICACEAAAAIIAICELEAACICIIGIGEAAAAAIGGAIATIAITAGAA 3451
                                                                                                                                                                                                                                                       3210 AACCAIAIGAIACIALCAIACIACIGAAACAGAFIICAFACCICAGAAIGIAAAAGAACI 3259
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Movel androgen receptur associated proteins used to detect androgenic
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Human, androgen recoptor coartivator, ASA54, APA55; APA24; detection;
Rb: androgenic; antiandrogenic; identification; prostate cancer; ss.
                                                                                                                             3572 AACCATATGALACTATCATACTACTGAAACAGATIICATACCTCAGAATGTAAAAGAACT
                                                                                                          3512 ACTIGTIGTIGTTTTTATAAAATTTTTGCTTTTTTAAATAAAAGCTGGAAGCAAAGTAT
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                                                                                                                                                                                                                                                                                                                               3270 TACHGAFTATTTTCTTCAFCCAACTTATGFTTTTAAATGAGGAFTATTGATAGT 3323
                                                                                                                                                                                                                                                                                                                                                   3632 TACTGATTATTATCTCCACCCAACTATGTTTTTAAATGAGGATAATGATATTGATGT 3685
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            or antiandrogenic activity in serecting assays for candidate pharmaceutical molecules which promote or inhibit the activity
                                                    /note= "androgen receptor coactivator"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Location/Qualifiers
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                                                                                                                                                                                                                                                                                                                                                                                                                                                           AA288441 standard; cDNA; 4839 BP.
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lacilitate the development of screening assays to evaluate the potential efficacy of drops in the freatment of prostate cancer.

Sequence 4839 BP; 1534 A; 902 C; 880 C; 1523 E; 0 other;

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.052 TGTAACATCTAATGGACTTCCAGGGTTGAAAATCTTTCTAAACGATAGGAAGAAGTTTA TTTT 1112 TOTTAAAAATAAAGATCTAGAAGATTATTTTTGGATCATGATAAAACTCTTCAGAC 1171 11/2 TGATPCTATAGACAGTTTTGAAACACAGAAAAACACACAAAAAAGTAACCTGATGATGAAGA 1231 92 MATGAGGGAAAAAAGHILIAH HGAAAAAH HIRIAGGTITTATGAATTCTCTTGGACT 1051 810 HGATTCTATAGACAGTTTTGAAACAGAGAAGACAGGAAAAAGGAACGTTGATGAGGA 869 (9) ATTACAAATGGAAGATCTGATCTGATTTCATTTCAGTTAATGCTATGTCTTGACTA 449 450 ITTLIATIAAACICICACCICCATGITGCTCAAAGAACCATATAAAACACCTGTTATACC 509 570 ACAACTAGAAAATGATACAAGAATTATTGAAGTTCTCTGTAAAGAACATGAATGTAATAT 629 630 AGALGAGGEGAAAAAHGELLALLEGAAAAFELTTALAPPOTTTATATGAAFEGTTGGAGT 689 690 TGTAACATCTAATGGACTTCCAGAGGTTGAAAATGTTTCTAAAGGATACGAAGAATTTA 749 750 TOTTAAAAATAAAGATOTAGAAGATATATTATTTTGGATOATGATAAAACTOTTCAGAC 809 452 TGCABCAGTEGACTASATGAGAIGTCGTTCACTTTACTGAGCTACAGAAAAACATAGA 511 ISU AATCAGTGTCGATAAATTGTTTAACTTACTAAAAGAAATTGATAGGAGTAGGAAGTGA 209 210 TAATGUTATGTCAAGACTGTTGAAGAAGTATGATGTATTGTTTGCAGTCTTCAGCAAATT 269 270 OGAAAGGAMATGTGAAGTTATATATTTGAGAGGAGGAGGTGGATATGTAGTGAAAT 329 532 GGAAAAGAATATGTGAAATITATATATTTGACAAAACCCAAGAATTCCAATATCTACTGAAAT 691 3.0) AAATTCTGGATGGTGCTAAAAGTTTCTTGGATCACATTTTTATTAGCTAAAGGGGAAGT 389 592 AAATEEGOATTOOLOGIACIAAAAGITTOTGGALGACAITTITTATEAGGAAAGGGGAAGE 751 510 CATTAATGGTTCACCTCGAACACCCAGGCGAGGTCAGAACAGGAGTGCACGGATAGCAAA 569 932 ACAACTAGAAAATGATACAAGAATTATTGAAGTTCTCTGTAAAGAACATGAATGTAATAT 991 512 AATCAGTGCATAAALTCTITAAGTTAAAAGAAATTGATAGCAGTACCAAAGTTGA HIZ TTTTATTAAAGTCTCACCTGCCATGTTGGTCAAAGAACCATATAAAAGAGCTGTTATAGC 97.1%; Score 4226; DB 21; Length 4849; 99.8%; Pred. No. 0; 5; Indels D: Mismatches Conservative Best Local Similarity Materines (4229)

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1532 AGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACATTTTTCATATGTC 1591 1230 ITTATIGGGGIGGGCTCTIGAGGTIGTAATGGCCACATATAGCAGAAGGTACATGTCAGAA 1289 1290 TCTTGALLCEGGAACAGALLGECTTECTALGGALTGEGAALGEGTLEAALLAAAAGT 1449 1652 TCTTGATTCTGGAACAGATTGTCTT1CCCATGGATTCTGAATGTGATTAATTTAAAAGC 1711 1410 AATGATAAAACATTTAGAAGGATGTGAACATCGAAATCATGGAATCCTTGCATGGTTCTC 1469 1650 TGCAAATGCAAAAGAACAAGCTCAGCCTTGCAGACCAAAAGCATTGAAATCTAG 1709 2010 AGAAGAGGAGTAYGATYCTATYATYGTATACYGTGG FCTTCAYGCAGAGACTGAA 2069 2070 AACAATATTTTGCAGTATGCTTGCAGGGGGGGGTTGCTTGTGACATACTTAGAT 2129 1110 ATACAAACTIGGAGTIGGIIGIALIACGAGTAATGGAATGCATGCTIAAATGAAAAA 1169 1656 CITIAAAGAGAAATITGCIAAAGCIGIGGAGAAGAIGIGIGIGIGGAAAIIGGALGAAAAGAGAAA 1109 1592 TITLAT LGGCGTGCGCTCTTGAGCTTGTAATGGCGACATATAGAAGTACTACTAGAA 1350 CTTTGATTTTTACAAAGIGALGGAAGILLIALGAAAGGAGAAAGGAATLGAGAAAAA 1470 AGATIFACCITTALITGAIGTIATIAAAGAATGAAAGGACCGAGAAGGACTGAEGA 1530 CCTTGAATCLGCTTGTCCTCTTAATCTTCCTCTCAGAATAATCACACTGCAGCAGATAT 1590 GTATCTTTCTCTCTGTAAGATCTCCAAAGAAAAAAGGTTCAACTACGCGTGTAAATTCTAC 1952 GIATCITICICCIGITAAGA ICTCCAAAGAAAAAGGI ICAACIACGGGGGAAAI ICTAC 1770 TIGTGAACGCCTTCTGTCTGAGCACCCAGAATTAGAACATATCATCTGGACCTTTTTCCA 2132 TTGTGAGGCCTTGTGTGTGAGGAGGCAGAALIAGAAGATALGATGTGGGAGGTLTTLTGA 1830 GCACACCCTGCAGAATGAGTATGAACTCATGAGAGACAGGATTTGGACAAATTATGAT 2432 AACAAAYATTITGCAGTA1GCT1CCACCAGGCCCCCTAGCTTGTCAATACCTCACTAT 1892 CCTTGAATCTGCTTGTCCTCTTAATCTTCTCTCTCGCAGAATAATGAGAGGAGGAGATAL 2012 TGCAAATGCAGAGACAAAGCAAGCTCAGAACCAGAAGAAGAAATGTAG 1710 CTCTCTTTCACTCTTTTTATAAAAAGTGTATCGGCTAGGGTATGGGGTAAGAGAAAAAA 1890 GEGEFICCAEGEATATGCAAAGEGAAATALAGAGGTTTAAATTICAAAATGALTGE 2252 GIGITICCA IGLATOCAA ATOCAAAGTGAAGAATAAATTAAATTAAAATAATTAAAATTAAA 1950 AACAGCATAGAAGGATGTTGCTCATGCTGTTCAGGAGACATTGAAACGTGTTTTGATA 2192 GCACACCCTGCAGAATGAGTATGAACTCATGAGAGACAGCAATTGCAACAAATTATGAT 9 <u>a</u> Š ŝ 9 Ś 3 ô â ŝ â ò g ŝ qq ें q qq ò q ò 9 ò <u>a</u> Š 9 <u>a</u> Š Š q ć ò Š

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11-5.2 CANTEGORTAGEGAATCCAAAAGAAAGTATACTGAAAAGAGGAGAGATATAGGATATAGAATACAT 1411

930 AATGATGATTTTAAAATTGAGGAAGTGATGAAGGTTGAGAAAATGTGATTTGGTATTTAA

1232 OTIGAATGIAATTOPTOPAGACTOCAGITAGGACTGITATGAACAGTATGCAACAATT 1291

B70 GUIGAARIGIAATTOOTOOACACACTOAGTAGGACTGITATGAACACTATGGAACAATT 929

3572 AACCATATGATACTATCATACTGAAAGAGATTTCAFACCTGAGAATGTAAAGAACT 3631 3270 TACLGATTATITTCTTCATCCAACTTATGITTTAAATSAGGATTATTGATAGT 3323 [11][11][11][11][11][11][11][11][11][11	RESULT 11 ABL62873 ID ABL52873 standard, DNA, 4839 BP.	XX XX XX 15-MAY-2002 (first entry)	Breast cancer related gene sequence SEQ ID NO:1210. Human; cancer, colon, breast; ovary, ocsophagus, kidney; t			13-DEC-2001. 30-MAY-2001;		20.SEP-2000; 20.SEP-2000; 20.SEP-2000; 22-SEP-2000;		25-SEP-2000; 25-SEP-2000; 25-SEP-2000; 26-SEP-2000;	25-SEP-2000; 27-SEP-2000; 27-SEP-2000; 27-SEP-2000;	27-SEP-2000; 28-SEP-2000; 28-SEP-2000; 28-SEP-2000;	28-SEP-2000; 28-SEP-2000; 29-SEP-2000; 29-SEP-2000;	24~SEP~2000; 02~0@r~2000; 02~0@r~2000; 02~0@r~2000;		03-OCT-2000; 03-OCT-2000; 03-OCT-2000; 03-OCT-2000;	01 - NOV - 2000) 01 - NOV - 2000)
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nan; cancer, colon, breast; ovary, oesophagus, kidney; thyroid;
omach; lung, prostate; panereas; carcinoma; antitumour; cancerous;
costatic, gene therapy, antineoplastic, Wilm's tumour, adenocarcinoma;
ast cander related gene sequence SEQ ID NO:1210.
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-JUN - 2000;
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(AVAL.) AVALON PHARM.

Carter RC, Ebner R, Endress G, Horrigan S; Support DR, Measure 1

WPI; Z002 188264/24.

chemical agent to be tested for anti-meoplastic activity, and determining a change in expression of a gene of a signature gene set. Screening for anti-neoplastic agent involves exposing cells to a

Maim 1; SEQ 10 1210; 44pp; English.

adenocarcinoma, carcinoma, clear cell cancer, infiltrating ductal cancer, infiltrating lobular cancer, squamous cell carcinoma, neuroendoczine carcinoma, papillary carcinoma and Wilm's tumour. anti neoplastic agent. The method involves exposing cells to a chanical agent to be rested for anti neoplastic activity, determining a change in expression of at least one gene (1) of a signature gene set, where (1) compises a sequence (8) selected from 844 Sequences (given in ABL51664 to ABL70110), or is at least 95% identical to (8), where a change in expression is indicative of anti-neoplastic activity. (1) has extostatic activity of and can be used for producing a product which is the data collected with respect to the anti-neoplastic agent as a structure and the data is sufficient to convey the chemical structure and/or properties of the agent. MI can be used in the trendical structure and/or properties of the agent. MI can be used in the trendical The present invention describes a method (MI) for screening for an oesophageal, ovarian, kidney, prostate or pancreatic cancer,

Sequence 4839 HP; 1534 A; 902 C; 880 G; 1523 T; 0 other;

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90 TOPTGAGGTGGAPCTAGATGAGATGTGGTTCACTTTTACTGAGCTAGAGAAAAAATAGA 149 452 100AGCASTTGACCTAGATGAGATGTCGTTCACTTTTACTGAGCTACAGAAAAACATAGA 511 150 ANTONTICICATAANTICITTAACTTACTTAAAAGAAATTICATAGGAAGTTIGA 209 512 AATGAGTGTGCATAAALTCLTTAAGTTACTAAAGAAATTGATACCAGTACCAAAGTTGA 571 572 JAATOCIATGICAAGACIGIIGAAGAAGIAIGATGITATTGITTGCACTCTTCAGCAAATT 631 270 OGAAAGGAGATGTGAATTTALATTTGAGACAACCAGCAGTTCGATATCTACTGAAAT 329 330 AAATTETGCALIGGTAAAAGTTGCTGGALGACATTTTTATTAACTAAAGGGGAAGT 389 752 ALLACAAALGGAAGALGALGLGALTICAITICAGTIAATGCTALGIGIGGTIGACIA 811 450 TELEALIAAACHCICACCCAGATGTECCAGAGAACCATATAAAAAAAGACETGTEAFACC 509 812 TITTATTAAACTOTOA CTOCOATGITGOTOAAAGAAGCATATAAAAGAGCTGITATACC 871 510 CALTAATGGTTCACCTTCGAACACCCAGGCGAGGTCAGAACAGGAGTGCAGGGATAGCAAA 569 97.1%; Score 3226; DB 24; Length 4839; 99.8%; Pred. No. 0; 5; Indels 0; Mismatches Matches \$229; Conservative Local Similarity Overy Match

570 ACAACTAGAAAATGATACAAGAATTATTGAAGTTCTCTGTAAAGAACATGAATGTAATAT 629

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1049 1470 AGATTCACCTTTATTTGATCTTATTAACAATCAAAGGACCGAGAAGGACCAACTGATCA 1529 1530 CCTTGAALCTGCTTGTCCTCTTGTTGTTCTCTAGAATAALCACACTGCAGATAL 1589 1590 GTATCTTTCTCTGTAAGATCTCCCAAAGAAAAAGGTTCAACTACOCGTGTAAATTCTAC 1649 992 AGATGAGGTGAAAAATGTTTATTTCAAAAATTTTATACCTTTTATGAATTCTCTTGGACT 10%1 1050 CITIAAAGAGAAATITGCIAAAGCIGIGGGACAGGIIGIGIGGAAATIGGAICACAGG 1109 1412 CTTTAAAGAAAATTTGCTAAAGCTGTGGGACAGGLTGTGTGGAAATTGGATCACAGGG 1471 1110 ATACAAACTIGGAGIICGCIICIAIIACCGAGIAAIGGAAICCAICCIIAAAICAGAAGA 1169 1170 AGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACALTTTTCALATGTC 1229 1532 AGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTCATATGTC 1591 1290 TCTTGATTCTGGAACAGATTTGTCTTTCCGATGGATTGTGAATGTGATTAATTTAAAAAGG 1349 1712 CITTGATITITACAAAGTGAAGGTTTTATCAAAGGAGAAGGCAACTTGACAAGAGA 1771 1772 AATGATAAAACATITAGAACGATGTGAACATGGAALGALGGAATGCCTTGCALGGCTCTC 1831 1650 TGCAAATGCAGAGACACAAGCACCCTCGCGCAGAGCCAAGAAGCCATTGAAATCTAC 1709 1710 CTCTCTTTTCACTGTTTTATAAAAAGTGTATCGGCTAGGCTATCTCTGGGGCTAAALACACT 1769 630 AGATGAGGTGAAAAAFGILIATTTGAAAAHIILAIAAGTILIAHGAAHITTGHGGACL 689 690 TGTAACATCTAATGGACTTCCAGAGGTTGAAAATCTTT/TAAACGATACGAAGAAAATTTA 749 1472 ATACAAACTIGGCTIGGCTIGGATTACGAGGAATCCATGCTTAAATCAGAAGA 750 TCTTAAAAATAAAGATCTAGATGCAAGATTATTTTGGATCATGATAAAAACTCTTCAGAC 810 FGAFTCTATAGACAGTTTTGAAACACAGAGAACACAGAAAAAGTAAAGTTTGALGAAGA 990. CAACTGGACAGTGAATGGAAAAGAAAGTATTGTAAAAGAGTGAAGGATATAGGATATAT 1410 AATGATAAAACAITTAGAACGAIGIGAACATCGAATCAIGGAATCCITGCAIGGCICTC 2012 TGCAAATGCAGAGACAACAACCTCAGCCTCCAGACCCAAGAAGCCATTGAAATCTAC 930 AATGATGATTTTAAATTCAGCAAGTGATCAAGCTTCAGAAAATCTGATTTCCTATTTTAA 1952 GTATCTTCTCCTGTAAGATCTCCAAAGAAAAAGGTTCAAGTACGGTGTAAATTTTAC q: q qq 9 q q ò g <u>a</u> ô ò õ ò $\dot{\circ}$ ò

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Diagnosis of retinoblastoma - using genetic material corresp. to a normal human retinoblastoma gene or a unique sub-region
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                                                                                                                                                                                                                       3210 AACCATATGATACTATCATACTACTGAAACAGAITTCATACCTCAGAATGTAAAAGAACT 3269
                                                                                                                                                                                                                                                                                                                    3152 TITTAAAAAGTIGTAGCAGATTGTTTCCTTCCAAAGTAAAATTGCTGTGCTTTATGGAT 3211
                       2970 TIAATITAACAIGAACACCCITAGAAAAIGIGICCIAICIAICTICCAAATGCAATITGA
                                                                                                                                                            3030 TIGACIGCCCATICACCAAAAITAICCIGAACICIICIGCAAAAATGGAIATTATIAGAA
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                                                                                                                                                                                                                                                        3150 ACTGTGTGTTGTTTTATAAAATITGCTTTTAALTAAAIAAAAGCTGGAAGCAAACTAT
                                                                                                                                                                                                                                                                                                                                                   3270 TACTGATTATTTTTTCTTCATCCAACTTATGTTTTTAAATGAGGATTATTGATAGT 3323
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Retinoblastoma; neoplasm; osteocarcoma; ss.
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337..2787
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Human retinoblastoma gene.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Dryja TP, Friend S;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        WPJ; 1988-065827/10.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                          AAN81369;
                                                                                                                                                                                                                                                                                                                                                                                                             RESULT 12
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This gene curedes a protein, the absence of which is associated with a needbash. It is used to produce an antibody to the protein, contacting this with the tumour sample and detecting immune complexes as indication of the presence in the tumour sample of the protein. Whole sequence or a unique sub-region can be used. The method identifies patients lacking the detective retinoblastoma (RD) allele and thus are not at risk of

775 FOLLAAAAALAAAGAFOLAGAFGCAAGAFFATHTEGGATGAFGAFAAAGFFGTGAGAGG 1034 1095 INTGAATGTAATTCCTCCACACACTCCAGAGTTAGGAGTTATGAACACTATCCAACAATT 1154 389 750 TOTTAAAAATAAAAATOTAAATATAATATTITTGGAFGATGAFAAAACTOTTGGGAC 809 BLO FGATTTTAAAGACAGTTTTGAAACAGAGAACACGAAAAAAGTAACGTTGATGAAGA 869 90 TCCTGAGGTCGACCTAGATGAGTTGTCGTTCACTTTTACTGAGGTAGAGAAAACATAGA 149 150 ANTORGEOGRAPHANTELLIANCELACABANGANALEGERACCAGANGER 209 AATCAGTGCCATAAATTCTTTAACTTACTAAAAGAAATTGATACCAGTACCAAAGTTGA 434 210 TAATGCTATGCGAAGACTGTTGAAGAAGTATGATGTATTGTTTGCAGTCTTTGAGGAAATT 269 270 GGAAAGGACATGTGAACTTATATATTTGACACAGCAGCAGTTGGATATCTACTGAAAT 329 555 AAATICTGCATTGCTGCTAAAAGTTTCIIGGATCACAITTTTATTAGCTAAAGGGGAAGT 614 190 ATHACAAATGGAAQATGAFCTGGTGTTTCAFFTTAATGGTAFGTGTGCTTGACTA 449 450 TITIATTAAAGTGTGGAGGTGGATGTTGGTGAAGGAGGATATAAAAGGGGGTGTTAIAGG 509 195 APARTIAGAAAA HALACAAGA HALIATIGAAG FIGIGIGIAAAGAAGAIGAA IGAATGIAATAT 1854 855 AGALGAGALGAAAAARGELTALLICAAAALITIATACCITITALGAATICTCGTGGACT 914 690 TGTAAPATPTAATBGAPTTPPAGAGTTGAAAATGTFFFFAAAGGATAGGAAGAATPTA 749 115 FGTAACATCTAATGGACTTCCAGAGGTTGAAAATCTTTGTAAAAGGATACGAAGAATTTA 974 870 GITGAATGIAAFTGITGAAGAGAGTGAGTTAGGACTGITATGAAGAGTATGAAGAATT 929 940 AATGATGATTITAAATICAGCAAGTGAFCAAGCTITCAGAAAATGIGATTICCLATTITAA 989 0; Caps 430 AAATTCTGCATTGGTGCTAAAAGTTTGTTGGATCACATTTTTTATTAGCTAAAGGGGAAGT TO CALLAATOOLICACOLOJAACACAGGGGGGGGGGGAGAGAGGGGGGGGGGGGATAGGAAA 195 GGABAGGACATGTGAACTTATATTTGACACCCAGCAGTTGGATATGTAGTGAAAT 6.30 AGA EGAGGEGAAAAARGITIATITEGAAAATITIATAGGITTIATGAATICICITIGGACI 97,0%; Score 3224,4; DB 9; Length 4597; 99,8%; Pred. No. 0; 6; Indels Sequence 4597 BP: 1489 A; 839 C; 815 G; 1454 T; 0 other; 0; Mismatches Matches \$228; Conservative developing the disease. Similarity | POC3 | 3 ž 5 ÷ 5 ŝ 5 ŝ 5 â $\stackrel{\sim}{\sim}$ ÷ 5 <u>-2</u> S = 5 = ŝ 5 $\frac{2}{\Xi}$ 5 1 5 â 5 $\stackrel{>}{\supset}$

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1275 CITIAAAGAGAAATITGCIAAAGCIGIGGGACAGGGIIGIGICGAAATIGGATCACAGGG 1334 1170 AGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACAACTTTTTCATATGTC 1229 1455 TTTATTGGCGTGCGCTCTTGAGGTTGTAATGGCCACATATAGCAGAAGTACATCTCAGAA 1514 1.44.9 1410 AATGATAAAACATTTAGAAGGATGTGAAGTGGAATGATGGAATGGCTTGGATGGTGTTG 1469 1530 CCTIGNATCTGCTTGTCCTCTTNATCTTCCTCCCAGAATAATCACACACACAGAATAT 1589 1155 AATGATTTTAAATTGAGGAAGTGATGAGGTTCAGAAAATGTGALHTGGGALHTAA 1214 1215 CAACTGCACAGTGAATCCAAAAGAAAGTATACTGAAAAGAGTGAAGGATATAGAATACAT 1110 ATACAAACTTGGAGTTGGCTTGTATTAGGGAGTAATGGAATGCATGGTTAAATGAGAAGA 1350 CTTTGATITITACAAAGIGATGGAAAGTTFIAICAAAGCAGAAAGGAACITGATAAGAAA 1575 CTTTGATTTTTACAAAGTGATCGAAAGTTTTATCAAAGCAGAAGCCAACTTGACAAGAA 1470 AGATTCACCTTTATTTGATCTTATTAAACAATCAAAGGACCGAGAAGGACCAACTGATCA 1815 GTATCTTTCTCCTGTAAGATCTCCAAAGAAAAAAGGTTCAACTACGCGTGTAAATTCTAC 1710 CTCTCTTTCACTGTTTALAAAAAGGGAAAGGGTAGCCTAICTCCGGCTAAATACACT 1770 TEGEGAACCCCTCTCTCTCTGACCACCAGAALLAGAACATALCALALCTGGACCCTTTTTCA 1830 GCACACCCTGCAGAATGAGTATGAACTCATGAGAAAAAGAGAATTTGAAATTATGAT 2115 GTGTTCCATGTATGGCATATGCAAAGTGAAGAATATAGACGTTAAAATTCAAAATCATGT 2010 AGAAGAGGAGTATGATTGTATATAGTATTGTATAACTGGGTCTTCATGGAGAGACTGAA 1050 CITHAAAGAAATITIGCIAAAGCIGBGAAAGGILIGIGIGGAAAA DIGGALAAAG TCTTGATTCTGGAACAGATTTGTCTTTCCCATGGATTCTGAATGTGTGATTTTAAAAGC 1755 COTTGAATCTGCTTGTCCTCTTAATCTTCCTCCAGAATAATCACACTGCAGATAT 1890 GTGTTCCATGTATGGCATATGCAAAGTGAAGAATATAGACCTTAAATTCAAAATGATTGT 1950 AACACCATACAAGGATCTTCCTCATGMTCTLCAGGAGAMATICAAAMATGTTTTGALMAA 2175 ANCAGGATACAAGGATCTTCCTCATGCTCTTCAGGAGACATTCAAACGTGTTTTGATCAA . g G G qq 9 ŝ á ò q q ò q õ q 9 <u>a</u> qq qq 9 ò G G ò â ò ò Ś 9 ò ò ô ŝ Š

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2775 GGAAGAGAAA GGAGGATCTCAGGACCTTGGTGGACATGTGTACACCTCTGGATTCATTG 2834
                                                                                                     21 5 TATTICACCO TGAAGAGICCAIATAAAAITICAGAAGGICIGCCAACACAAAAAI 2249
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AANAAATATTIIRGAGIATGCFFGGAGGGGGGGGGGTAGCTTGTGAGGAATACCTGAGATI 2129
                                                                                                                                                                                                                                                                                                                                                                                      2130 FORTGGAAGGCTTTAGAAGTTTFGCTAGTTTGAGGGGTTTGGTGGGATTGGTGGGAAGAGATGTA 2189
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J.GAGJIGGGGALIGACCAAAALIAFGGTGAACTCTTGTGCAAAAATGGAFALTATTAGAA 33.14
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3210 AACCATATGATACTATCATACTACTGAAACAGATTTCATACCTCAGAATGTAAAAGAACT 3269
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              o: Caps
3150 ACTGTGTTGTTTTALAAATTTTGCLTLAATAAALAAAAGCTGGAAGGAAGIAL
                                3435 AACCATATGATACTATCATACTACTGAAACAGATTTCATACCTCAGAATGTAAAAGAACT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         presence of the protein in the sample. The method may be used in
the detection and treatment of a defective human gene related to
                                                                                                                                                        3495 TACTGATTATTTCTTCATCCAACTTATGTTTTAAAIGAGGATAATGATA <548
                                                                                                                                    3270 TACTGATTATTITCTTCATCCAACTTATGTTTTAAATGAGGATTATTGATAGT 3323
                                                                                                                                                                                                                                                                                                                                                                                                Retinoblastoma; cancer, detection, diagnosis; protein; neoplasm;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              97.0%; Score 3224.4; DB 15; Length 4597;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    compating genetic material corresponding to a normal
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Diagnosing the presence of defective retinobiastoma alleles
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               6, indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Sequence 4597 RP; 1489 A; 841 C; 912 G; 1455 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   human retinoblastoma with DNA from a patient.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             0; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            (MASS-) MASSACHUSETTS EYE & EAR INFIRMARY. (WHED ) WHITEHEAD INST BIOMEDICAL RES.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Example 2(2); Figure 7: 18pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          cancer, in particular retinoblastoma.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Location/Qualitiers
                                                                                                                                                                                                                                                        AAQ70536 standard; DNA; 4597 BP
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                                                                                                                                                                                                                                                                                                                                                                Human retinoblastoma gene.
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AATGAGTGFCATAAATTGTTTAACTTAAAAAAATTGATACCAGTAGGAGTGAAAATTGATAACTGAAAAGTTGAAAAGTTGAAAAGTTGAAAAGTTGAAAAGTTGAAAAGTTGAAAAAGTTGAAAAAGTTGAAAAATTGAAAAAA	OGAAAGGACATGTGAACTTATATATTTGACAAGCCGGGGGGTTCGATATCTACTGAAA FILLICICICILICILICICILICICILICILICILICIL	AAATICTEE ATTEETEETTAAAAGTITCTTGGGTCATATTTTATTAGTTAAAGGGGAGG	TTTTATTAAACTCTCACCTCCCATGTTGCTCAAAAAACGATATAAAACAGTTTTTTTT	CATTAATGGTTCAPYTCGAAAACCAAGGGAAGGTCAGAACAAGAAGGATGYACGGAT 	AYAAYTAGAAAATGATAYAAGAATTATTGAAGTICICIGITAAAGAAYATGAATGI. 	AGATGAGGTGAAAAAGGTTAATTCAAAAATTTAAAGGTTTAATGAATTCFCTEGAC FELLELLELLELLELLELLELLELLELLELLELLELLELL	HGTAACATCTAATGGACTFCCAGAGGTGAAAATCTTTCTAAACGATACGAAGAAATTT. FFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	PULBAAAAAAAAATU BAATOGAAGA PATTITOGATCATGATAAAACTCTTCAAAC FELLITELLE BELLITELLE STELLE TELLITELLE TELLITELLE BELLITELLE TELLITE TCTTAAAAATAAAGA CSTAGATGGAAGATTA TELLITEGATCAFGATAAAACTCTTCAGAC	PARTICTATA APARTAGITT BAAACA CADAGAA WOODGGAAAAAAGTAAPOTTGATGAAGAA ELLELLI LI	OSTGAATGTAATTOOTPOAGAGTCAAGTTAAGACTGTTATGAAGACTATGGAAAAT 	AALGALGATTI AAALIPAGTAAGIGALCAAGGI ICAGAAAA ICTGATTITOGI ATTTI AA ELELELELELELELELELELELELELELELELELELE	C'AN'TOCAC'AGGAATCCAAAAGAAGTATACTGAAAAGAGTGAAGGATATAGGATATAGGATTATAGGATATACTGAAAAGAAAG	AAA!AGAAATTTGCTAAAGCTGTGGGACAGGTTGTGTCGAAATTGGATCACAGGG 	ATAPAAAPTEGGAGTEGGTEGTATTAPGGGGTAATGGAATGG	AGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTCATATGTC 	TTTATTGGCGTGCGCTCTTGAGGTTGTAATGGCCACATATAGGAGAGTACATCTCAGAA
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210 1AA1 210 1AA1 445 TAA1		555 AAATTCT 850 ATTACAA		510 CATT	570 ACAA	6.40 AGAT	636 TGT/ 1111 315 TGT/	750 PCFF 	810 F;AI	870 GGTC 	930 AATC	990 CAAC 1111 215 CAAC	1050 CTTTAA 	1110 AIAG	1170 AGAZ 1111 1395 AGAZ	1230 TTTA
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οy	1290	TCTTGATTCTGGAACACATTGTCTTTGCCATGGATTCTGAATGTGCTTAATTTAAAAGC 1449
qu	1515	TCTTGATTCTGGAACACATTTGTCTTTCCCATGCATTCGAATCTGCTTAATTTAAAACTTS74
λō .	1350	CTTTGATTTTACAAAGTGATGGAAAGTTTTATCAAAGGCAGAAGGCAACTTGACAAGAGA 1409
Ω Ω	1575	CITITGATTITITACAAAGIGATGGAAAGTTTTATCAAAGCAGAAGGCAACTTGACAAGAGA 1634
Oy	1410	AATGATAAAACATTTACAACGATGTGAACATGGAATCATGGAATGCCTTGTC 1469
ģ. ;	1635	AATGALAAAACATTIAGAAGGAIGIGAACATGGAATTATGGAATCCCTTGTATGGCTCTC 1694
	1695	470 AGALICACCIITATTIGALI ITALIAAACAALAAAGAA GAGAAGAA CAATAALAA 1729
ò	1530	CCTTGAATCTGCTTTTAATCTTCCTCTCTCTCAGAATAATCACACTGCAGAATAT 1589
ସ୍ଥ	1755	CCTTGAATCTGCTCTTTAATCTTCCTCTCCAAAAAAAACACTGAAAAATAATCTAATATTAATCTTGCTCTCAAAAAAAA
oy o	1590	GTATCTTCTCCPGTAAGACTCCAAAGAAAAAAGGTTCAACTACGTGTAAATCTTAC 1649
<u>a</u>	1815	GTATCTTCTCCTGTANGATCTCCCAAAGAAAAAGSTTCAACTAGGGGTGTAAATTCTAC 1874
ž 2	1875	TOLAMETOL AGMARTA MAST MACTITAGO TICTAGO TAGAGOTA TOMAGATA MOTAGO I III II HILLI II HILLI HILLI HILLI HILLI HILLI HILLI HILLI HILLI HILLI TOCAMTOCAGAGACAACCAACCAACCICAGOTITO AGMOTAGAACCA IGAAA ICLAAA
Ĉ	1710	CTCTCTCTTTTTTATATATATATATATATATATATATAT
g g	1935	
ô	1770	TIGIGAACGCCTTC (CICLGAGCACCCAGAAL LAGAACA J.A.C.).
qq	1995	TIGEGARGSCTTCTGTGTGTGTACCAGAATAGAACATAGATGTGTGTGT
Qy	1830	GOACACCCTGCAGAATGAGTATGAACTCATGAGACAAAAAAAA
ପ୍ତ	2055	GCACACCCTGCAGAATGAGTATGAACTCATGAGAGAGAGA
ò	1890	GTGTTCCATGTATGGAAAATGGAAAGATGAATATAGACCTTAAATTCAAAATCATTGT 1949
q	2115	GIGTICCATCIATIOCATATICCAAAGIGAAGAATATATATATATAAAATATATATATATATA
ΟŸ	1950	AACACCATACAAGGATCTITCLCATGCTGTTCAAGAGATATICAAACGTGTTTTGATAA 2009
qq	2175	AAGAGCATACAAGGATCTTCCTCATGCTCTCAGGACATCTTCAAACGTCTTTTGATCAA 22.44
ОУ	2010	AGAAGAGGAGTATGATTGATTATAGTATTGTATAAPTPGGTCTTCATGTAGAGAGTGTGA 2069
g G	22 15	AGAAGAGAGIATGATTGIATAGIATTGIATAAGTOGGIGTTGATGAGAGAGTGAA 2294
ò	2070	ANCANAIRTITISCASIAISCITECACTAGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG
qa	2295	AACAAATATTTGGAGTATGCTTGCAGGAGGCCGCTAACTTGTCAGCAATACTTGAGT 2354
OY	2130	TCCTCGAAGCCCTTACAAAGTTTCCTAGTTCACCTTACGGATTCCTGGAGAAAATCTA 2189
વા	2355	TCCTCGAAGCCCTTACAAGTTTCCTAGTTCACCCTTACGGATTCCTGGGGGGGAACATCTA 2414
οy	2190	TATTTCACCCCTCAAGACTCCATATAAAATTTCAGAACTCTCCCACCAACAAAAAT 2249
qo	2415	TATTICACOCOTIGAAGAGI CCATATAAAATI LCAGAAGGI CTGCCAACACAACAAAAAT 2474
ογ	2250	GACTCCAAGATCAAGAATCTTAGTATCAATTGGAAATTGGGGAACTTGTGGAGAAGTT 2369
qu	2475	GACTICLAND CARGATIC THE FINANCIA CATTICLAND CONTROLL OF THE CATTICL OF THE CATTIC
Οy	2310	CCAGAAAATAAATCAGATGGTATGTAACAGCGACCGTGGGTCAAAAGAAGTGTGTGAAGG 2369
Dp	2535	CCAGAAAATAAATCAGATGGTATGTATGTATGTTTTTTTT

Human retinoblastoma gene cDNA.

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24++ TESTACTEGAACACGAATGCAAAAGCAGAAAATGAATGATAGCATGGATACCTCAAACAA 2549`
AAGCAAGGG1GGTAAAGCAGTGAAAAAGTAGGGTTTTGATATTGAAGGATGAGATGAAGG 2429
                        259 AAACAACCIICTAAACCACIGAAAAAATTAACTITTAATATIGAAAGAICAAATGAAGC 2654
                                                                                                              24.40 AGATGGAAGTAAACATCTCCCAGGAGAGTCCAAATTTCAGCAGAAACTGGCAGAAATGAC 2489
                                                                                                                                                                     26/5- ANATIGGAAGTAAACAFCTCCCAGGAGGTCCAAATTTCAGCAGAAACTGGCAGAAATGAC 2714
                                                                                                                                                                                                                                                                                   2715 TELLACICIAAPAPAPAPAPAAPPAPAAAFIGAAFIGAAFIGAFIGAFIGGAFAPPITAFIAPPAPAAFAA 2774
                                                                                                                                                                                                                                                                                                                                                2550 GGAAGAGAAA EGAGGATCTCAGGACCTT GGTGGACACTGTGTAGAGGTGTGGATTGATTG 2609
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AAX04501 standard: cDNA: 4597 BP

RESOLUTION 14 AAXO4501 (first entry)

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deletion or point mutation in the Rb gene of a human patient. The gene can also be used to synthesize Rb polypeptide (see AAYD1542) for use in the treatment of individuals determined to have a detective
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             150 AATCAGTGTGCATAAATTGTTTAACTTAQTAAAAQAAATTGATAGCAGTAGGAAAGTTGA 209
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             analysing predisposition to retinoblastoma and for the detection and
                                             Potinoblastema; Ph gene; human; predisposition; diagnosis; therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  chromosome 13 lambda phage library, was used in a chromosome walk in solute and map 30 kb of genomic DNA surrounding the HT-8 sequence. Fragment P7H30.78 (ATC 97500) was obtained, and was used as a probe to screen a cDNA library that had been constructed from an adenovirus 12-transformed human embryonic retinal celline. This provided clone p4.78 (ATC 9738), which in Northern blots cross-reacted with a 4.7 kb transcript, in transformed retinal cells which was not present in 4 retinoblastoma and one osteosarcoma cell samples. Rb nucleic acids compitaing the Rb genc, cDNA or a fragment of the genc, such as one of the 27 excus or 26 introns, can be used in a claimed method for detecting a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    retinoblastoma gene Rb. Absence or mutation of the Rb gene (see also AAX04502) predisposes an individual to retinoblastoma. To isolate Rb cDNA, the human DNA probe pH3-8, isolated from a human
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Isolated human retinoblastoma gene · used to develop products for
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         97.0%; Score 324.4; DB 20; Legalls 1597; 99.8%; Pred, No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      This is the nucleic acid sequence of a cDNA of the normal human
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           6; Indels
                                                                                                                                                                                 'transl_cxcrt' (pos:2632..2634, da:Asp)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 4597 BP; 1489 A, 841 C, 813 G, 1454 T; 0 other;
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(WHED ) WHITEHEAD INST.
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86US-0895163.
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                                                                                                  Homo sapiens.
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210	TAATOOTATO CAAGACTGI TGAAGAAGTATGATTGTTTGCTTGCACTCTTCAGGAAATT 3 	269 494
435	A EGHGAATTI ATATA HIGAPAPAPAPAPA HIGALIH GAAATTI AGHGAAATTI HILLIH GAAGATTI GAATTI AGAAATTI A	329 554
555	TRETOCATTOCTOCTANANGTTCTOGATCACATTTTATATACCTANAGGGAAGT 	389 614
490 615	ALTAYAAALOGAAGALGAL/LOGIGALII/CALII/GAGITAAIGCFALGFGFGCFTGACTTGACTA ATTAYAAATGGAAGAAGGGAGATTTCATTTCAGTTAAFGCFATGFGFGFGTGACTTGACT	449 674
450	FITTATTAAAAA CHO PAYO PYO ATOTTOCHGAAAGAACCATATAAAAACAOCHGTTATACCOTTITTATTATTAAAACACCATATAAAAACAOCHGTTATACCOTTITATTAATAAAACAOCHGTTATACCOTTAATAAAACAOCHGTTATACCOTTAATAAAAACAOCHGTTATACCOTTAATAAAACAOCATATAAAAACAOCHGTTATACCOTTAATAAAAACAOCATATAAAAACAOCATATAAAAACAOCATATAAAACAOCATATAAAACAOCATATAAAACAOCATATAAAACAOCATATAAAACAOCATATAAAAACAOCATATAAAAACAOCATATAAAAACAOCATATAAAAACAOCATATAAAAACAAAAAAAA	509
510	AAA SAAA	569
570 795	ATAT	629 854
6.40 8.55	3ACT	689 914
04.4 81.8	TUTANCATCTAATGBACTTCCAGAGGTGAAAATCTTCTAAAGGATAGGAAGAAATTTA TEELEELEELEELEELEELEELEELEELEELEELEELEEL	749 974
750	PTTAAAAATAAAGGTOTAGATGGAAGATTATTTTGGATGATGATAAAGTGTTGAGA HTTTTTTTTTT	809 1034
810	DATECTA FASACASTELLEAAACACACACCACGAAAAACHAACCELGATGAAGA F ELLELLELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTELLETTE IGALICTA FAGACASTELLGAAACACAGAAAAACTAACCETGAAGA	869 1094
1035	GOTGAAFGTAATTCCTCCACACTCCAGTTAGACTGTTATGAACACTATCCAAAATT (FEELELEELEELEELEELEELEELEELEELEELEELEELE	429 1154
9.40	A H	989 1214
990	CAACHONACAGIGAARCCAAAAGAAAGTATAN TGAAAAGAGIGAAGGATATAGGATAGAT TITTITTITTITTITTITTITTITTITTITTITTITTI	1049
1050	CTITAAAGASAAATITG TAAAGTGTGGGGAAATIGGTGGGAAATIGGTACAGGG TELLE CLEELELELELELELELELELELELELELELELEL	1109
1110	ATACAAACTTGGAGTEGGTEGTATTACCGAGTAATGGAATCCATGCETAAATCAGAAGA 	1169
1176	A GAARGA HATCHA BORAAA HII AQCAAACHCHGAATGACAACA HTTHCATATGTC TITTHA HATTHA BORAAA HATTHA HATTHA HATTHA BATTA CAATGACAACA HTTHCATATGTC AGAAGAA HATCCA HCAAAAA HATAOCAAACHCTGAATGACAAAAA HATGTC	1229
1230	TTTATTGGGGTGTGTGAGGTGTAATGGGCACATATAGAGAGAAGTACATCTCAGAA 	

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                    1515 TCTTGATTCTGGAACAGATTTGTCTTTTCCCATGGAATGTGGTTAATTTAAAAG: 1574
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1290 TCTTGATTCTGGAACAGATTIGTCTTTCCATTGGATTCLGAATGIGCTTAATTIAAAAGC 1349
                                                                               1350 CTTTGATTTTACAAAGTGATCGAAAGTTTTATCAAAGCAGAAAGGAAACTTGACAAGAA
                                                                                                   1470 AGATTCACCITTATITGAICTIATIAAACAALCAAAGAAGGACCGAGAAGGACCAACIGAICA
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2370 AACCAACCTCCTAAAACACTCAAAAAATTACCTTTGALATTGAAAGGALTAGAAGGT 2429

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                                               25.95 AAGGAAGGTGCTAAACCACTGAAAAAGTACGCTTTCATAFTGAAGGATCAGATGAAGC 2654
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327- FACTGATTATTTTTTCTTCATCCAACTTATGTTTTTAAATGAGGATTAFTGATAGT 3323
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Modified retinoblastoma tumour suppressor gene

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protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                proliferation, particularly cancers. The RTSPs have a broader spectrum of activity than wild type RTSPs.
             Modified retinoblastoma tumour suppressor, RTSP protein, caneer therapy,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        HITTATTAAACTCTCACCTCCCATGTTGCTCAAAGAACCAIATAAAACAGTGTAAAC, 740
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               270 GGAAAGGACATGTGAACTTATATATTTGACACCCAGCAGTTCGATATCTACTGAAAT +29
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     330 AAATICIGGATIGGTGGTAAAAGTTTGTTGGATGAGATTTLATIAGGTAAAGGGGGAAGT 389
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          mbis sequence erecdes a medified retio.blastoma tumbut suppressor
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular prollieration, particularly cancer
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Sequence 3554 BP; 1170 A; 683 C; 653 G; 1048 T; 0 other;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Claim 22; Page 226 230; 249pp; English.
                                 cellular proliferation inhibitor; ss.
                                                                                                 Location/Qualifiers 7..2793
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                                                                                                                                                                                                                                                                                                                                  (BAYU ) BAYLOR COLLEGE MEDICINE
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                                                                      Homo sapiens.
                                                                                                                                                                                                                                                         19-FEB-1998;
                                                                                                                                                                                                                                                                                             20-FEB-1997;
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CATTANTOGEN AND LEGERACIAC CAGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGAAA	ACAACTAGAAAATGATACAAGAAFTATTGAAGTICTCTGTAAAGAACATGAATGTAATTTTTTTTTT	NGA EGAGOTGAAAAA TOTTA TATATAAAAAA TATAA COTTATA EGAAATTO TOTTAGGACT EEFELEELEELEELEELEELEELEELEELEELEELEELEE	TGIAACATCTAATGGACTTCCAGAGTTGAAATCTTTCTAAAGGATACGAAAATTTA -	POTTAAAAA LAAAAGU LAGA LGDAAGATTA LITTI LGGATCATGAAAAC FCTTCAGAC 	TGATTCTATAGACAGTTTGAAACACAGAAAAAAAGAAAAGGAACAGAAAAAAAA	OGIGAATGIAATTCCTCPACACACHCAGITAGGACIGITATGAACACTATCCAACAATT - - - - - - - - - - - - - - - - - -	AATGATGATTI AAATTOAGAAGGAAAGCI CAGAAAA CYGALI IGGI ALTITAA TILLI II LITTI TILLI II LITTI GILLI ELI LITTI LITTI LITTI LITTI LITTI AATGATGATGATGATGAAAATGGATTTGAAAATGATTAAA	FANCTOCRERAGO RANAGARANGA ANA GARARARA GARARA GARARA BARARA BARAR	CTTTAAACAGAAATTTGCTAAAGCTGTGBBACAGGGTTGTGTGGGAAATTGGATCACAGGGG 	ATACAAACTIGGAGTICOTTIGTATIACCGAGTAATGGAATCCATGCTTAAATCAGAAGA 11) IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	AGANGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTGATATGTC FFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	TITATEGGGGGGGGCTCTIGAGGTEGTAATGGCCACATATAGCAGAAGTACATCTCAGAA 	CCT DATECTOGAACAGATTOTCTTT CCATGAATCTGAATGTGCTTAATTTAAAAGC FEEFFELLEETTTTTTTTTTTTTTTTTTTTTTTTTTTTT	CTTTGATTTTTACAAAGTGATCGAAAGTTTTATCAAAGCAGAAAGGCAACTTGACAAGAAA CTTTGATTTTTTTTTT	AAFGATAAAACATTAGAACGATGTGAACATGGGAATCCCTTGCATGGCTCC	ADALICAPO ELLA HEGALO HA HAAAQAA CAAAAGAGGGAAGGAAGGACGAAGTIGATGA HILLIH AVAATGAAAGGACGGAGAAGGACGAACGAACGAACGAAGGAAG	CCTIGAATCTGCTIGTCCTCTTAATCTTCCTCTCCAAATAATCAACGCGCGCGC	GTATCTTTCTCCTGTAAGATCTCCGAAAAAAAAGGTCCAACTAGGGGGGAAATTCTACTTTTTTTT
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Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular prollieration, particularly cancer
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        P-FSDB; AAW69473.
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protein (KTSF) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cannots. The RTSPs baye a broader spectrum of activity than wild type RTSPs. This Sequence encodes a modified retinoblastoma tumour suppressor

3161 BP: 1037 A: 619 C: 586 G: 919 T: 0 other

龙	equence 3161 BP; 1037 A; 619 C; 586 G; 919 T; 0 other;	
7.512	100.0%; Score 3161; DB 19; Length 3161; Lord; Similarity 100.0%; Brod No. 0.	
Matches	3161; Conservative 0	:0
ŝ	- GOGTCATGCGGCCAAAAAACCCCCCAAAAAACGCCCCAACGCCCACGCGCGCGCGGCG	
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ŝ ŝ	 (a) GARGCCTGGCACCGCCGCGCGCCCCCCCCCCCCCCCCCCC	
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<u>.</u>	401 TGGGGAALCTGTATTTTGCAGCAGTTGACCTAGCTGTTATACCCATTAATGCTTCA 360	
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5	12. GALACAASAATTAFIGAAGTICICIGTAAAGAACATGAATGIAATAFAGAFGGAGGAGAA 480	
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2.5	181 AAIGELIALITCAAAAATTTTATACCITTTATGAATTCTCTTGGACTTGTAACATCTAAT 540	
100	481 AAIGITTAITTCAAAAATTTTAFACCEFFTATGAATTCTCTTGGACTTGTAACATCTAAT 540	
ŝ	541 GGACITCCAGAGGITGAAAATCITICTAAACGATAGGAAGAAATTATCTTAAAAATAAA 600	
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q.	61 AGTEFFGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	
20	221 CCTCCACACTCCAGTTAGGACTGTTATGAACACTATCCAACAATTAATGATGTTTA 780	-
ac	721 CCLCCACACACACTAGACTGTLATGAACACTATCCAACACAATTAATGATGTTTA 780	

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1081 GCTCTTGAGGTFGTALGGCCACACATATAGCAGAAGIACALCICAGAATGTTGATTCTGGA 1140
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                                                                                                                                                                                                                                                                                                                                                                                           961 GITCGCITGTATTACCGAGTAATGCATGCTTAAATCAGAAGAAGAAGATTATCC 1020
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 1261 TTAGAANGATGTGAANAFNGATGATGAAATNONTWGATGGGTGTGAGATTGACCTTTA 1320
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                                                  781 AATTCAGCAAGTGATCAACCTTCAGAAAATCTGATTTCCTATTTAACAACTGCACAGTG 840
                                                                                                       841 AATSTAAAAGAAAGTAIAGTSAAAASASSAIAAAGGAIACATTAAAAGAAA 900 HIHHHHHHHHHHHHHHHHHHH
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                                                                                                                                                                 841 AATETAAAASAASTATASTSAAAASASIGAAGGATATAGSATACATSTTTAAAGASAAA
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GATICIA I PARA TATACHA TATACHA TERMINI TATACHA ANA AATATATATA	PAGIA DELLI COMPAGGOPO O PAGETIGIO MADOMATACCICACA HICCICIAAGGCGI HILLI HILLI HILLE HILLI KAAGCCCI CANTATGCTI CCAC WASSCOCCIACCITGI CACCAATA CCTCA. ATTOCCACA	TAFANSTITECTAGFICACECTAGGGATTCCIGGAGGGAACAFCTATATTICACCCCTG FILEFELFELFELFELFELFELFELFELFELFELFELFELFE	ANGAGEGCATATAAAATETCAGAGAGETGCGAACAGCGACCAAAAATGACEGCAAGATCA 	AGAALCTIAGIALPAATIGGIGAALPATIGGGACTICIGAGAAGTECAGAAAATAAAT HTITITITITITITITITITITITITITITITI MAATCTTAGTAGTAGATGATIGAATCATICGGGACTTCTGAGAAGTTCGAGAAAATAAAT	CPIATOGTATEITACAGGGGCEGTGTGCTCAAAGAAGGAGGTGCTGAAGGAAGCAAGCTCTCCT FELFIEFFEFFEFFFFFFFFFFFFFFFFFFFFFFFFFFF	AAAY GACTSAAAAAAY TACSCTITGATATGAACGATCAGATGAAGGAGAGTGGAAGTAAA 	CALCHCCAGGAGGCCAAATHCAGCAGAAACTGGCAGAAHGACHCTACTGGAAAT FEELLEELEELTITTETTETTETTETTTTTTTTTTTTTTT	CGAATICAAAAGCAGAAAATGAATGATAGCATGGATACCTCAAACAAGGAAGAGAAATGA 	GRAFOTO/ARRACTTGGTGGACACTGTACACCTCTGGATTCATGTGTCTCTCACAGATG	FOAM BOTALAACHT FOO AGD FIOTGTHA FOOD CACACATTAATALCH CAGGGGTFTTTTT FILLE FELLE FELL	GFGFATATAAAATGFGCAGAFGCAATTGFTTGGCTGATFGCTAAGGGAGTFGAAATGTT 	GFCATTGITATTTATACAGATTGAAAATCTTGTGAAAATCCTGCCATTTAAAAAGTTGT 	O'NG AGAING THE CHOT CAAAGTAAAA HGCTGTGCTTTATGATAGTAAGAATGCCC THEFFILLER CHILLER HELLER G O'N AGAINGETTGCTGTAAAATGCTGTGTGCTGTGCTTATGGATAGTAAGAATGGTC	CTANAGEGRAGITOCEGATAACOCAGROCIGICIGACIACI LIGOCITOTITIGIAGAT ELLELELELELELELELELELELELELELELELELELE	ATAGGGAGGHEGATCHGHHITATTAALHAIGHAIGHATATTTTTTAATTTAAGATG 	AAYAGGTIAGAAAADGIGGGTAGTAGTIGGAAAIGGAATTIGATIGAGTGGCCAT 	CACCAAAATTATCCTGAACTCTTGTGCAAAAATGGATATTATTAGAAATTAGAAAAAAT 	TW TAATTTTACATTACATTTATTTTACTATTGGAATCTGAFATACTGTGGTGTGT
		TACAAGETTOCTAGETCAGEGE ELGLELLILLITITITITITITI TACAAGETGGEAGELGAGOOT	AAGAGTCCATATAAAATTTCAG 	AGAALCETAGTATCAALIGGTG - - - - - - - - - - - - - - - - - - -	CAGATGGTATGTAACAGGACC 	AAA CACTGAAAAAA TACSCT TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT					01004141411111111111111111111111111111		ANCAGA FIGETITOCIO FIGGAA THEFFILLE SHELLELLE ARCAGATTOTTOCAGA		ATAGGIGALGI 15,C101 [611] 	AACACCTTAGAAAATGTGTCCTCTTTTTTTTTTTTTTTT		
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This sequence encodes a modified retinoblastoma tamour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting callular proliferation, when coadministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular prollleration, particularly can eefs. The RTSPs have a broader spectrum of activity than wild type RTSPs.
                                                                                                                                                                                                                                                                                                                                                                                                 Modified retinoblastoma tumour suppressor; RISP protein; cancer therapy;
                                                                                                             2941 TACTAATTITACACATTAGATTITATTIACTATIGGAAICTGATATACTGIGIGGAG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                61 GAACCCCCGGGCACCGCCGCCCCCCCCCCCCGGGGGGCCCCAGAGCACAGGACAGCGGC 120
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                            3001 TITATAAAATTITGCITITAATTAAATAAAAGCIGGAAGAAAAGTATAACALATGATAC
FELLITITITITITITITITITITITI
3001 TITATAAAATTITGCITITAATTAAATAAAAGCIGGAAGGAAAGTATAACAATATGAAA
                                                                                           3061 TATCATACTACTGAAACAGATTTCATAGCTCAGAATGTAAAAGAACTTACTGATTATTTT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     93.88; Score 2965; DH 19; Length 347;
94.48; Pred. No. 0;
Live 0; Mismatches 0; Indels 186;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Sequence 3347 HP; 1096 A; 650 C; 617 G; 984 I; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                inhibiting cellular prointeration, particularly cancer
                                                                                                                                                          3121 CTTCATCCAACTTATGTTTTTAAATGAGGATTATTGATAGT 3161
                                                                                                                                                                           Modified retinoblactoma tumbur suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Claim 22; Page 196-200; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                cellular proliferation inhibitor; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Location/Qualifiers
7..2586
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                                                                                                                                                                                                                                                                     AAV58448 standard; DNA; 4347 BP
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Matches 4161; Conservative
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1141 CTTGGAGTFGGCTTGTATTACCGAGTAATGGAATCCATGCTTAAATCAGAAGAAGAACGA 1200 2221 CCCCTGAAGAGTCCATATAAATTTCAGAAGTCTGCCAACACACAACAAAAAATGCCA 2280 1015 TTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTCATATGTCTTTATTG 1074 1195 TTTTACAAAGTGATGGAAAGTTTTATCAAAGGAGAAGGGAAAGTTGACAAGAGAAATGAIA 1254 1255 AAACATITAGAACGATGIGAACATCGAATCATGGAATCCCTIGCATGGCTCTCAGATTCA 1314 2161 AGGCPTFACAART FOLAGFFCAACT CAACAACAAGAAAGACAACAAA 2220 1375 TCTGCTTGTCCTCTTAATCTTCCTCTCCAGAATAATCACACTGCAGAGATATGTAFCLL 1434 2035 CCCCTGAAGACTCCATATAAAATTTCAGAAGGTCTGCCAACAACAACAAAAATGACTCCA 2094 1075 GEGGEGETETEGAGGIEGIAAAGGEETEGAGAGAGAGAGAAGAAGAAGAAGAAGAAGAAGAAATGITGAT 1135 TCTGGAACACATTTGTCTTTTCCCATGGATTCTGAATGTGCTTTAATTTAAAAGCCTTTGAT 1315 CCTTTATTTGATCTTATTAAACAATCAAAGGACCGAGAAGGACCAACTGATCACCTTGAA 1435 TELECTGIAAGA CIECDAAGAAAAAGGIICAACIACGGIGIGAATICIACIGOAAAT 1555 TCACTGTTTTATAAAAAGTGTATCGGCTAGACTATGTGGGGGTAAA1AGACTTTGTGAA 1615 GGGTICIGICIGASCACCASAATIASAACAIATCATCIGGACCCITIECCAGCACACC 1861 CTGCAGAATGAGTATGAACTCAIGAGAGAGACAITIGGACCAAAIIAIGATGIGTCC 1735 ATCTATGGATATGGAAAGTGAAGAATATAGACCTTAAATTCAAAATCATTGTAACAGCA 1795 TACAAGGATCTTCCTCATGCTGTTCAGGAGACATTCAAACGTGTTTTGATCAAAGAAGAG 1855 GACTATGATTCTATTAGTATTCTATACTCCGTCTTCATGCAGAGACTGAAAT 1915 ATTITICCAGITATICACITICEACCOCCCTACCTTGTCACCAATACCTCACATTICCTCGA 2101 ATTITIGCAGTATGCTTCCACCAGGCCCCTTACCTTGTCACCAATACCTCACATICCTCGA 1975 AGCCCTTACAAGTTICCTAGTICACOCTTACGGATTCTGGAGGGAAGATCTATATTICA 1621 TCFCCFGTAAGAFCTCCAAAGAAAAGGTTCAACFACGGGTGTAAAFTCTACFGCAAAF 1675 CTGCAGAATGAGTATGAACTFATGAGAGAGAGATTTGGACCAAATTATGATGTTCC 1981 TACAAGGATOLIOALOADOAGAGATOAAAAGGTGTTTTGATGAAAGAG 1495 GCAGAGAGAAAGAAGTIGAGGGTIGGAGAGGCAGAAGCCATTGAAATGTACCTGTTT .⊙ ••• q C ò υp g 9 ò qq òλ ò q q οy g ò 五 ζý Ω qq Qqq Οy q

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2095 AGATCAAGAATCELIAGIAALIGAALIGGIGAALCATTGGGGACTTCTGAGAAGTTCCAGAAA 2154
                                                                                                               2155 ALAAATPADALGDIALGTAAPAGGAGGIGTGGTCAAAAGAAGTGGTGAAGGAAGAAG 2214
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                                                                                                                                                                                                                                                                                                                     Modified retinoblastoma tumour suppressor; KTSP protein; cancer therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                121 CCGGAGGACCTGCCTCTCCTCAGGCTTGAGTTTGAAGAAACAGAAGCTGATTTTACT 180
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             inhibiting cellular proliferation, particularly cancer
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QY 10b	1165	CTGAARGEGCTTAATTTAAAAGGCTTTGATTTTTACAAAGEGAAAGTTTTATCAAA 1224
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Oy Db	2195 2401	OTOCTOAAAAQAAGTGCTGAAGGAAGCAACCTGCTAAACCACTGAAAAAAACTAOSTTTT 2244
δ	2245	GATATTGAAGGATCAAGAAGGAAGGAAGTAAAGATCTCCCAGGAGAGTCCCAATTT 2304

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2461 GATATTGAAAGATCAAAGAAGCAAGAAGTAAACAACAACAAATTT 2520
                                                                         2.465. GATAGGATGGATACCTCAAAGAAGGAAGAAATGAGGATGTCAAGGAGGTTGGTGGACAC
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                                                    2305 CAGCAGAACTGGCAGAAATGAGTTGTAGTGGAACGAATGGAAAAGGAAAATGAAT 2364
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protein (RISP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p54 protein. The RISPs can be used for treating diseases characterised by abnormal cellular
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         prollheration, particularly cancers. The RTSPs have a broader spectrum of activity than wild type RTSPs.
                Modified retinoblastoma tumour suppressor, RTSP profesor, cancer therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         317 TTATTGCAGCAGTTGAGCTAGCTGTTATACCCTAATAATGCTTCACCTGGAACACCGAGC 476
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           377 GAGGECAGAACAGGAGGGGGGGATAGCAAAACAACTAGAAAATGATACAAGAATTATTG 436
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              329 GAGGIICAGAACAGGAGTGCACGGATAGCAAACAAGTAGAAAATGATACAAGAATTATIIG 388
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            617 TATITITIGGATCATAAAACTCTTCAGATTGATTCTATAGACAGTTTTGAAACACAG 676
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              89.4%; Score 2827.4; DB 19; Length 3113; 99.6%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                         Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
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2537 CAGATGCAATTCTTTGGGTGATTCCTAAGCCACTTGAAATGTTAGTCATTGTTATTTTATA 2596 2549 CARGATTGAAAATCTTGTGTAAATCCTGCCATTTAAAAAGTTGTAGCAGAGTTGTTTCTC 2608 2289 CTCTCTATCTATCTATCAAATGGAATTGATTGATTGACTGCCATTCACCAAAALTALCCTG 2848 2849 AACTCTTCTGCAAAAATGGATATTATATAATAAAAATTAGAAAAATTACTAATTTTACACAT 2908 1769 TTCAGGAGACATTCAAAGGTGTTTTGATCAAAGAAGGGGGTAGGGTCTAFTATAGTAT 3828 1877 ICTATAACTCGGTCTTCATGCAGAGTGAAAAGAAATATTTTGCAGTATGCTTGCAGCA 1936 1829 TCTATAACTCGGTGTTGCAGAGAACAAAGAAATATTTTGGAGTATGGTTTGGAGGA 1888 2117 TIGGIGAATCATICGEGACTICTGASAAGTICCAGAAAATAAATCAGATGGIATGIAACA 2176 2417 GTGGACACTGTGTACACCTCTGGATTCATTGTCTCTCACAGATGTGACTGTATAACTTTC 2476 2477 CTAGGTTGTGTTTALGGCCACALTIANIALCTICAGCICITITGTGGGANIAIAAAATGTG 2536 2489 CAGATGCAATTGITTGGGTGAITCCTAAGCCACTIGAAATGTTAGTCATTGITAITAIA 2548 2597 CAAGATIGAAAATCTIGIGIAAAICCTGCCATTIAAAAAGITGIAGCAGATLUTTIGGIG 2656 2777 CTTGTTTTTTATTATTTTATATGTATTTTTTTAATTTTAACATGAACACCCTTAGAAA1 2836 2897 AACTCTTCTCCAAAAATGGATATTATTAGAAATTAGAAAAAATTACTAATTTTGGGAL 2956 1937 GGCCTTACCTDGTCACTAATACCICACALICCTCGAAGGCCCTTACAAGTTGCTAGH, 1996 1997 CACCCTTACCGATTCCTGGAGGGAACATCTATATTICACCCCTGAAGAGTCCATATAAAAA 2057 ITTCAGAAGGTCTGCCAACAACAAAAATGACTCCAAGATCAAGAATCTTAGTALCAA 2009 TTTCASAAGGTOLGGGAAGAGGAAGAAAAGGCICCAAGATGAAGAATCTTAGTALGAA 2177 GCGACCCTICTICAAAAGAAGFCFFFFAAGAAGGAAGFFFFFFFAAAAGGAGTAGTAAAAAAAG 2129 GGGACGGGGGGGAAAAGAAAGGGAAGGCAAGGAAGCCTCCTAAACCACTGAAAAAAC 2189 TACOTTTGATATGAASSALCASALGAASCAGAAGTAAACATCLOCCAGGAGG 2249 PCAAATTTPAGGAGAAAPTGGPAGAATGAPTTGTAGTGGAAGAGGAA FGGAAAAGYAGA 2357 AAATGAATGATAGCATACCTGAAAQAAQGAAGAGAAATGAGGATGTCAGGAGTIG 2657 IIVVAAASTAAAAITGTGTGTGTGTGGGATAGATAGAAATGGGGTAGAGIGGGAGIGGT 2717 GATAACCCAGGCCTGTCTGACTACTTTGCCTTCTTTGTAGCATATAGGTGATGTTTGCT 2729 CITICTITITATITATITIATATICTATATITITITAATITIAACAIGAACACCCITAGAAAAL 2837 GTGTCCTATCTATCTFCCAAATGCAATTIGALTGGCCGATCGCCATCACCAAATTATCACC 2237 TACCOTTTGATATTGAAGGATCAGATGAAGGAGATGGAAGTAAACATGTGGCAGGAGAGT 2609 TPPCAAAGTAAAAPTGCTGTGCTPTAPPGGATAGTAAGAAPGGCGCTAGAGTGGGAGTGCT 40 q O qq ò جَ ď ò g qq qq Ch õ qq

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lines in which gene expression is tightly regulated by Lettacycline. They can be used for the production of proteins such as tumour suppressor proteins which can be used for treating diseases characterised
                 2969 TTTAAFTAAATAAAAGCIGGAAGCAAAGTAFAACCAFATGATACTACTACTGAAA 3028
                                                                                                                                          1077 CAGATTICATACCTCAGAATGTAAAAGAACTTACTGATATTITCTTCATCCAACTTATG 3136
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        The present sequence appears in the specification, which describes a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         transactivation domain (TTD) operatively attached to a telracycline repressor protein (TRP), the first sequence operatively positioned downstream of a permoter, the vector also contains a cloning site operatively positioned downstream of a basal promoter exemptising a tetracycline operator. The TREVs can be used to produce stable cell
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         tetracycline responsive expression vector (TREV), which contains a sequence encoding a lusion protein comprising a transcriptional
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Minimal promoter; retracycline responsive expression vector; TREV;
                                                                    3017 TELAATFAAATAAAAGCEGAAAGTATAACCATATGATACTATCATACTACTGAAA
2957 TAGATELTALPITAGIA I LGGAATOLGATATACTO IGTGOTI GETTATAAAAAFTTTGOT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                New fetracycline responsive expression vectors - used for the tightly controlled expression of genes, such as tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          transcriptional transactivation domain; TTD;
tetracycline repressor protein; TRP; tetracycline operator;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           by abnormal cellular proliferation, particularly cancers.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            productions stable cell line; protein production;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              tumour suppressor protein; treatment; cancer; ss
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                                                                                                                                                                                                                                    4089 TTTTTAAATGAGGAFTATTGATAGT 3113
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                                                                                                                                                      374 TCAAAGAACCATATAAAACAGCTGTTATACCCATTAATGGTTCACCTCGAAGACACAGGC 433
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                                                                                                                317 FFATFOGAGGAGFFGAGCFAFFAGGGAFFAAFGGTFFGAGGFGGAGAGAGAGGG 376
                                                                                                                                                                                               377 GAGGTCAGAACAGGAGTGCACGGATAGCAAAACAACTAGAAAHGATACAAGAATTTATTG 436
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Sequence 3218 HP; 1080 A; 595 C; 561 C; 982 T; 0 other;
                                                                           Matches 2834; Conservative
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                                              1347 AATGAAAGAGGGAGAAGGAGGAAGTGATGAGTTGAATGTGGTTGTGTGTTAATGTTG 1396
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Modilied retinoblasiona tumour suppressor; «TSP protein; vanoer therapy)
                       3134 CAGATITICATION TOTAGAAATGAAAGAACTTACTGATTATTTCTTCATCCACTTATG 3193
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2417 CHGGACACTGTACACCTCTGGATTCATTGTCTCTCACAGATGTGACTGTALAACTTTC 2476
                                                                                       2477 CCAGGITTCTGTTTTTGGCCACATTTAATATCTTCAGGTCTTTTTGTGGATATAAAAIGIG 2536
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protein (RESP) of the invention. The proteins can be used for inhibiting cellular profiteration, when coadministered with a p53 protein. The RESPs can be used for freating diseases characterised by abnormal cellular.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        89.4%; Score 2827.4; DB 19; Length 3266;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            0; Mismatches 11; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Sequence 4266 BP; 1092 A; 502 C; 574 G; 998 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   unhibiting cellular profiteration, particularly cancer
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                                                                                                                                                                                                                                                                                                      (BAYU ) BAYLOR COLLEGE MEDICINE (TEXA ) DNIV TEXAS SYSTEM.
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917 GACAGGGTTGTGTCGAAAFTGGAFCACAGGAFAYAAAYTTGGAATFFGTTGTATTATTATTATT
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                                                                                                                                 22.47 TACGOTTTGATATTCAAGGATCAGATGAAGGAAGTAGAAGTAAAGTATCTCCAGGAGGAGT 2295
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protein (RTSP) of the invention. The proteins can be used for inhibiting cellular prolliferation, when coadministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Modified retinoblastoma tumour suppressor, RTSP protein; cancer therapy;
3182 CAGATITICATACCTCAGAAATGIAAAAGAACTIACTGATTATTTTTTCTTCCATCCACTTATG 3241
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Modified retinoblactoma tumeur suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                0; Mismatches
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          cellular proliferation inhibitor; ss.
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                                                                                                      3137 ITITIAAATGAGGATTATTGATAGT 3161
                                                                                                                                                                              3242 TITITIAAATCAGGATTATIGAIAGI 3266
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Ha S, Xu H, Zhou Y;
                                                                                                                                                                                                                                                                                                                                                                AAV58443 ctandard: DNA; 3323 BP.
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17.59 ATGGGCTAGCCTATCTCCGGCTAAATACTTTGTGAACGCTTCTGTGTCTGAGACACCTAG
                                                                                              1799 AATTAGAACATATCATCTGGACCCTTTTCCAGCACCCTGGAGAATGAGTATGAACTCA 1858
                                                                                                                                                                                                                1257 AGAATATAGAGGITAAATICAAAATGATIGITAAGAGGATACAAGGATCTICCTCATGTB16 1816
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                                                         1637 AATTAGAACATATCATCTGGACCCTTTTCCAGCACACCTGCAGAATGAGTATGAGTCA 1696
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Meditica retinoblastoma tumout suppressor, KTSP protein, camber therapy, relimiar proliferation inhibitor; ss.
                                                                      281 / TESSAMASTANANTSSTSSTSSTSSTSSSATASTANSANTSSSSSTSSASTSSSASTSSSASTSSS
                                                                                                                                                                                                                                27.77 CITGITITATTAATTTATATGTATATTTTAAATTTAACATGAACACGCCTTAGAAAAT 2836
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       §§17 TITAATTAAATAAAAGCIGGAAGCAAAGTATAAGGATATGATACTAATTAATTAATAGTAAA 3076
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Modified retinoblastoma tumour suppressor, KTSP protein, cancer therapy;
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                                                                                                                                                                                                                                                                                                                                                                                                                                      Modified retinoblastoma tumour suppressor, KISP protein; cancer therapy:
                                                                                                                                    317 TEATTGCACCACTICACCTACCTCTTATACCALTAATGCTTCACCTCGAACACCACGC 376
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    611 TCAAAGAACCATATAAAACAGCTGTTATACCCATTAATGGTTCACCTCGAACACCCAGGC 670
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               188 TAGATITIATITIAGIAATGIGAATGIGATALAGGIGGGIGGITGITITATAAAATTITGAT
                                                                               8248 ITTAATTAAATAAAAGCTGGAAGCAAAGTATAAACATATGATACTATCATACTAAAA
                                                                                                                3077 CAGATITCATACCICAGAAIGTAAAAGAACITACIGATIATITICITCATCCAACITATG
                                               8017 TEFFAATTAAATAAAAGCTGGAAGCAAAGTATAAGCATACTACTALCATACTGAAA
89.4%; Score 2827.4; DB 19; Length 3455; 99.6%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Retinoblastoma suppressor protein with N terminal modification
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Sequence 3455 BP; 1153 A; 631 C; 627 G; 1044 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                     Modified retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Claim 22: Page 142-147; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                      cellular proliteration inhibitor; ss.
                                                                                                                                                                                 3137 TITITAAAIGAGGATTATIGATAGI 3161
                                                                                                                                                                                                      3368 TTTTTAAATGAGGATTATTGATAGT 3392
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TCTATAACICGGTCTTCATGCAGAGACTGAAAACAA,AIJTGGAGTATGCTTCCACCA 1936
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                                                                 1517 CCTTCCAGAGCCAGAAGCCATTGAAATCTACCTCCTTTCACTGTTTTATAAAAAGTGT 1576
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Modified retinoblastoma tumour suppressor; RISP protein; cancer therapy;
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This sequence encodes a modified retinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p54 protein. The RISPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
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                                                                                                                                                                                              Meditied retinoblastoma tumour suppressor, RISP protein, cancer therapy,
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Metinoblastoma suppressor protein with N terminal modification inhibiting cellular proliferation, particularly cancer
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                                                                                                                                Modified retinoblastoma tumour suppressor gene
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0; Mismatches
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                                                                                                                                                                                                                                     religiar proliferation inhibitor; ss
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Matches 2834; Conservative
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                        977 GAGTAATGGAATGCATGCTTAAATCAGAAGAAGAAGATTATATAGTATTTTAGTA 1036
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627 GAACACCACAAAAAAATAAACCTTGATGAAGTGAATGTAATTGTTGTACACA DG AG 736
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1753 AGAATATAGGTTAAATTTCAAAATGATTGTAAQAGGATAAAAAGGATGTTGTTAT
                          2.4.9 GGCCCCTACCTTGTCACCAATACTCCTCGAAGCCCTTACAAGTTCCTAGGT 2389
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                                                                                                                                                                                                                                                                                                             1947 GOCCCCTACCTTGTCACCATACCTCACATTCCTCGAAGCCCTTACAAGTTTCCTAGTT 1996
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protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  proliferation, particularly cancers. The RTSPs have a Lecader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Modified retinoblasions tame at suppressor, RISE protein; cancer therapy; cellular proliferation inhibitor; ss.
                                                                                                                                                                                                                                                            3470 CAGATTTCATACCTCAGAATGTAAAGAACTTACTGATTATTTTTCTTCATCCAACTTATG 3529
2897 AACTCTTCTGCAAAAATGGATATTATTAGAAATTAGAAAAAATTACTAATTTACAAT
                                                                                                                                                                                          3077 CAGATTICATACCTCAGAATGTAAAAGAACTTACTGATTATTTTCTTCATCCAACTTATG
                                                                                                                                                                           3017 TTTAATTAAATAAAAGCTGGAAGCAAAGTATAAGCA1A.GA1ACTA.GA1ACTACAAA
                                                                            3290 AACTICTTCTGCAAAAATGGATATTATTAGAAAFTAGAAAAAAATTACTAATTTLAGAGAT
                                                                                                          3350 IAGAITTTATTTTAGTATTGGAATCTGATALACIGIGGGGGTGTTTAIAAAATTTTGCI
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Modified retinoblastoma tumeur suppressor gene.
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                                                                                                                                                                                                                                                                                                        3137 TTTTTAAATGAGGAFTATTGATAGT 3161
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4%; Score 2827.4; DB 19; Length 4555; 6%; Pred, No. 0; . 0; Mismatches 11; Indels 0; Gaps 0;	TOTTATACCCATTAATGGTTCACCTCGAACACCCAGGC 37	AGAAAATGATACAAGAATTATTG 43 	GGTGAAAATGTTTATTTCAAAA 49 HILLILLILLILLILLILLILL GGTGAAAATGTTTATTTCAAAA 88	FTCCAGAGGTTG 5	AGATGCAAGAT 61	FITTTOGATCALGAFAAACTCTFCAGACTGATFCTATAGACACTTTTGAAACACAGA 676 FITTTTGATCATGATAAAACTCTFCAGACTGATTCTATAGACAGATTTGAAACACAGA 1069	CCTTGATGAGAGGGGAATGTAATTCCTCACACACACAG 736 511 11 11 11 11 11 11 11	CAACAATTAATGATGATTTAAATTCAGCAAGTGATC 	ICLOATH CLIAITH AACAACHGCACAGHCAAHCCAAAAGAAAGHA 1856 - FELFELLI HELLI HELLI HELLI HELLI HELLI HELLI HELLI HELLI - COGATTOCHATITTAACAACHGCACAGAGAA CCAAAAGAAAGA 1249	IDATAGSATACATCTTAAAGAGAAAKTTGCTAAAGCTGTGG 916 	12 GACAGGETGTGTGGAAATTGGATGAGATACAAACTTGGAGTTGGACTGTATTAGC 976 	JAAATCAGAAGAAGAAGATTATCCAFTCAAAATTFTAGCA 1036 	IGAATGACAAYATTIITCAIATGICIIIAITGGGGGGGGGGGGTGITGAGGTAA 1096 	GOCNATALNICATANA TANA TANA TANA TANA TANA TANA TAN	PALGRAHICHGAANGETHAANHAAAAGGCHIGAFTTTIACAAGGGGGGGAAAGT 1216 FELLIHTHILHHITHHILEHHILEHHILHHIHHHIHHHIHHHIHHHI CARGAFEGGAATGTGATTAAHHAAAGGCHIGAFTTFRCAAAGGGGGGAAGGT 1609	vittgacaagaaatgataaacaithagaagagagagaac 1276 Hillililililililililililililililililili	TECATGRETETCAGATTCACCTTATTGATCTTATTAAAC 1336 	ACCAACTIGATICACTITICAATICTICCTICTTAATICTTIC 1396
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2057 TITICAGAAGGICTGCCAACAACAAAAA GACTTCCAAGAICAAAAICIIAGIAICAA 2116
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                                                                              1790 CTCTCCAGAATAATCACACTGCAGCAGATALGTATCLTTGTCCTGTAAGATCTCCAAAGA 1849
                                                                                                                                              1850 AAAAAGGTTCAACTACGCGTGTAAATTCTACTGCAAATGCAGAACACAACAAACTCAG 1909
                                                                                                                                                                            1517 CCTTCCAGAPCCAGAGCCATTGAAATCTACTTCTTTTGACTGTTTATAAAAAGTGT 1576
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                                                                                          2870 CCACCITETALGCCCACATTAALATCTTCACCTCTTTTGTGGGALATAAAATGTG 2929
                                                                                                                                                                                                                                                        2990 CASCATTCAAAATCTTGTGTAAAATCTTGACATTTAAAAAAGTGGTAACAGTTGCTC 3049
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                                                                                                                                                                                     2930 CAGALGCAA FEGITTEGGEGATTEGTAAGGGAGTTEGAAATGITAGTGATTGTTATA 2989
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                                                                                                                                                                Location/Qualifiers
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They can be used for the production of pioteins such as fullour suppressor proteins which can be used for treating diseases characterised
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               437 AAGTTCTCTGTAAAGAACATGAATGTAATATAGAGGGGGGAAAAATGTTTATTTCAAAA 496
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   tetracycline responsive expression vector (TREV), which contains a sequence encoding a fusion protein comprising a transcriptional transactivation domain (TED) operatively attached to a tetracycline repressor protein (TRE), the first sequence operatively positioned downstream of a promotor. The vector also contains a cloning site operatively positioned downstream of a based promoter comprising a tetracycline operator. The TREVs can be used to produce stable cell lines in which gene expression is tightly regulated by tetracycline.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                The present sequence appears in the specification, which describes
                                                                                                                                                                                                                                                                                                                                                                  tightiy controlled expression of genes, such as tumear suppressor
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                                                                                                                                                                                                                                                                                                                                               New tetracycline responsive expression vectors - used for the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       by abnormal cellular preliferation, particularly cancers.
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Best Local Similarity 99.6%; Pred. No. 0;
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2837 GIGTCCIATCTACCTCCAAATGCAATTTGATTGACTGCCCATTCACCAAAATTATCCTG 2896 1997 CACCCTTANGGATTCCTGGAGGGAACATCTATATTTAANNYCTGAAGAGTCNATATAAAA 2056 2057 ITTCAGAAGGTCTGCCAACAACAACAAAAATGACTGCAAGAATGAAGAATCTTAGTATGAA 2116 2237 TACGCTTTCATATTGAAGGATCAGATGAAGCAGAAGATGAAAGTAAAACATCTCCCAGGAGAGT 2296 2297 CCANATTCAGGAGAAACTGGGAGAAATGACTTCTACTGGAAGAGGAATGGAAAAGAAA 2456 2357 AAATGAATGATAGCATGGATACCTCAAACAAGGAAGAAGAAATGAGGATCTCAGGACTTG 2416 2477 CCAGGTTCTGTTTAIGGCCACAITTAATAICTICAGCTCTTTIIGIGGAIATAAAATUTG 2536 2537 CAGATICCAATTGTTTTGGGTGATTPTCTAAGGGAGTFGAAATGTTAGTTGTTATTATA 2596 2930 CAGATGCAATTGTTTGGGTGATFCCTAAGCCACTFGAAATGTTAGTCATTG1TATTTATA 2989 2990 CAAGATIGAAAATGITIGTGAAATGCTGCCATITAAAAAGITGTAGAAATHGITHGTC 3049 3110 GAIAACCCAGGCCIGICIGACIACTITGCCTTTTGTAGCATAFAGGTGATGTTGCT (169 2777 CITGITITATIAAITIATATGIATATTITITITAATTIAACAGAAACACCTIAGAAAAT 2836 2270 ICTATAACTCGGCTTCATGCAGAGTGAAAAAAATALLIGCAGTALGCLLCCACCA 2329 1937 GGCCCCCTACCTTGTCACCAATACCTCACATTCCTCGAAGCCTTACAAGTTTCCTAGTT 1996 2330 GGCCCCTACCTTGTCACCAATACCTCACTTCCTCGAAGCCCTTACAAGTTTCCTAGTT 2389 2390 CACCCITACGGATTCCTGGAGGGAACATCTATATTTCACCCTGGAGGGCCAIAIAAAA 2449 2450 TTTCAGAAGGTCTGCCAACACCAACAAAATGACTCCAAGAATGAAGATCTTAGTATCAA 2509 2750 AAATGAATGATAGCATGGATACCTCAAACAAGGAAGAAATGAGGATCTCAGGACCTTG 2809 2417 GTGGACACTGTGTACACTGTGGATTCATTGTCTCTCACACATGTGACTGTALAACTFTC 2630 TACCCTTTCA FATTCAAGG FCACATCAACCAGA FGGAA 11 AAACATCT COO AAGAAAT 2597 CAAGATTGAAAATCTTGTGTAAAATCCTGGCATTTAAAAAGTTGTAGCAGATTGTLC-TC 2657 TTCCAAAGTAAAATTGCTGTGCTTTATGGAIAAGAAAGGGCIAGAAGGAGTT 2717 GATAACCCAGGCCTGTCTGACTACTTTGCCTTCTTTTGTACATATAGGTGATGTTTGC 3290 AACTCTTCTGCAAAAATGGATATTATTAGAAATTAGAAAATTACTAATTTACAT 2957 TAGATITIATITIACIATIGGAATCIGATATACICIGIGGGTGGTTGTTTATAAAATTTTGCT ò Ś G qq ć 3 ŝ d ò ò 9 ć g Š qq ò ò qq Š qq ò ā ŝ â Ś qq à $\overset{\circ}{1}$ ò qq ć 5 ŝ 9

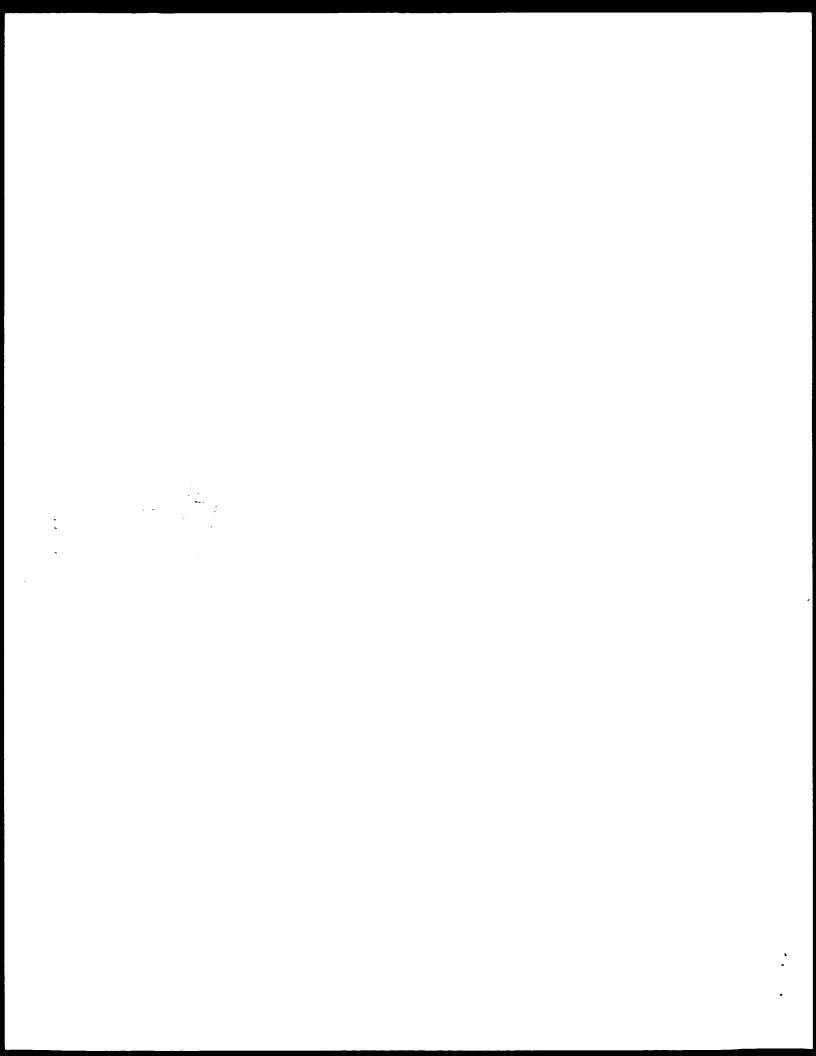
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sital componentia which hyposses khool/or p53. Antisense constructs of the kbool p161NK4a genes may also be used. The methods are useful for increasing the proliferative capacity of cells. The cells are subsequently of use in pharmaceutical and cosmetic preparations used to treat conditions related to (premature) agains, e.g. macutar degeneration.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            MESTL, telomerase, catalytic subunity reverse transcriptase, life span, retinoblastoma; p53; tumour suppressor; inhibitor; arterioscierosis; profiferation, immortal; tumour therapy; macular degeneration; activator;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  action the number of miletic discussions, of a cell. The method relies on action of a followerse series; of a cell. The method relies on action of a followerse series; yet a p53 pathway Phosphorylation of Rb by eyelin-dependent Kinases, edg and edgk, releases the relis into the division cycle. Hinding of INVA family members, e.g. the tumour suppressor p161NK4a, inhibits kinase activity and results in growth arrest. Rb Enactuations can selectively and results in growth division of Rb Enactuation and receivably inactivate an Rk CBF4 piber. Rb Enactuation of Rb-PiffINK4a pulbway. The energiate an analysis a cellular inhibitor of Rb-PifFINK4 pulbway. The energiate in RBC is a cellular inhibitor of Rb-PifFINK4 pulbway. The energiate in the methods other molecules which can be used in the methods. Other molecules which can be used in the case and mass are easier and resistant is one which dillers from a new more easier.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               New method for increasing the proliferative capacity of cell lines comprises administering agents reversibly activating telemerase activity and reversibly inactivating Rb/INK4 and/or p53 pathways useful
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        and arteriosolerosis. The rells can also be used to replace tumour cell
                                                                                      3410 ITHAAFITAAATAAAAGCTGGAAGCAAAGTATAACCATATGATACTATCATACTACTGAAA 3469
                                                                                                                                                                                                                                        3017 ITTAATTAAATAAAAGCTGGAAGGAAAGTAIAAGGAATAIGATACTATGATAGTAAGTAGTAAAA 3076
                                                                                                                                                                                      3077 CAGAITICALACCICAGAAIGTAAAAGAACTTACTGATTATTTTCTTCATGCAACTTATG 3136
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Additional constructs include a papilloma virus E7 protein, or other
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                                                                                                                                                                                                                                                                                                                                                                                           4137 TITTAAALGAGGATTATTGATAGT 3161
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lines in vitto and for studies on biochemical and physicionical aspects of growth and differentiation. Long lived (immortal) cells could also be of use in the production of normal or genetically engineered biotechnology products.
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nucleic search, using trame_plus_p2n model M protein

January 16, 2003, 23:41:58 : Search time 255.954 Seconds (Without alignments) 7011.280 Million cell updates/sec Ruth offi

US 09 026-459A-45 Title: Perfect score:

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BLOSUM62 Scoring table:

Xqapop 10.0 , Xqapext Ydapop 10.0 , Ydapext Phapop 6.0 , Fhapext Delop 6.0 , Delext

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Prod. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

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3.1	3683	88.9	3323		AAV58446	Modified retinobla
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<u>ب</u>	3550	85.7	3233		AAQ72690	Retinoblastoma 94k
36	3550	85.7	٠,		AAV58444	Modified retinobla
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ALIGNMENTS

PESULT 1 AAV58449 AAV56449 standard; DNA; 3161 BP

AAV58449;

(lirst entry) 02-DEC-1998 Modified retinoblastoma tumour suppressor gene.

Modified retinoblastoma tumour suppressor; KTSP protein; cancer therapy; cellular proliferation inhibitor, ss.

Homo sapiens

Location/Qualifiers 7..2400 /*tag-

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protein (RTSP) of the invention. The proteins can be used for inhibiting calculated proliferation, when coadministered with a ps3 protein. The BTSPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RTSPs have a broader spectrum of activity than wild type RTSPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             8] ValSerSerValAspClyValLeuGlyGlyTyrIleGlnLysLysLysGluLeuTrpGly 100
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                                                                                                                                                                                                                                                                                                                                                                                                           This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                 Revinoblastoma suppressor protein with N-terminal modification - inclibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Sequence 3161 BP; 1037 A; 619 C; 588 G; 919 T; 0 other;
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                        LysGluScrIleLeuLysArgValLysAspileGlyTyrIlePheLysGluLysPheAla 300
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161 TyrPheLysAsnPheIleProPheMetAsnSerLeuGlyLeuValThrSerAsnGlyLeu 180
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                                                                                                                                                                                     GlambralnArgThrProArgTysSerAsnLeuAspGluGluValAsnValIleEroPro
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Modified retinoblasiona tumour suppressor; RTSP protein; cancer therapy;
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This sequence encodes a modified retinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p54 protein. The KTSPs can be used for treating diseases characterised by almormal cellular proliferation, particularly cancers. The KTSPs have a broader spectrum of
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profein (RISP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p54 protein. The PTSPs can be used for treating diseases characterised by abnormal cellular
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                                                           Modified retinoblastoma tamour suppressor: RISP protein; cancer therapy;
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                                                                                                                                                            427 AGTACCAAAGTIGATAATGCTATGTCAAGACTGTTGAAGAAGTATGATGTATTGTTTGCA 486
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/note= "kb protein"
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                                                                              400 GlyAsnLeuThrArgGluMetIleLysHisLeuGluArgCysGluHisArgTleMetGlu 428
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769 LystenAlaGluMetThrSerThrArgThrArgMetGluLysGluLysMetAsuAspSer 788
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       regulating certain physiological processes of the body, such as
                                                                2527 AAACI GG YASAAATGA TICTA TICTAS TOGAASAAAAAGGAAAAAAGAAAATGAATGATA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       blood cell prodn. and gamete prodn. Fragments of the protein are
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           RB gene product, p56RB portion; cell cycle progression control; combination; therapeutic methods; arrest; tumourigenesis; requiation, physiological processes; blood cell produ.;
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7 to	21	ProAlaProProProProProProProGluGluAspProGluGluAspProGluGluAspProGluGluAspProGluGluAspProGluGluAspProGluGluAspProGluGluAspProGluGluGluGluGluGluGluGluGluGluGluGluGluG	roGluGluAspProGlu	SinAspSerGlyProGlu	40
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ā	613	CLETTCAGGAAATTGGAAAGGACATGTGAACTTATATATTTGACAGAGGCAGGTCG	GTGAACTTATATATTG	ACACAACCCAGCAGTTICG	678
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19f2	679	ATATCTACTGAAATAAATTCTGCATTGGTGCTAAAAGTTTCTTGGATCACATTTTATTA	TGGTGCTAAAAGTTTCT	FGGATCACATTTTATTA	738
2.0	110				110
101	7.49	GCTAAAGGGGAAAGTATTACAAATGGAAGATGATGTGGGTGATTTCAGTTAATGGTA	AAGATGATCTGGTGATT	CATITCAGITAAIGCIA	798
70	110				110
e e	449	POTICHECAL ICACLATITIA LI AAACHOT CACCTOCCATIGTTIGCT CAAAAAAAGAAGCATATAAA	TCTCACCTCCCATGTTO	CTCAAAGAAGCATATAAA	858
79. 21.	111 859	AlaValileProlikAsnGlySerProArqThrProArqArqGlyGlnAsnArgSer 	erProArgThrProArg 	ArgGlyGlnAsnArgSer [][][][][][][][][] 3GAGGTCAGAACAGGAGT	129 918
70	-		snAspThrArqllelle	31 uVal LeuCyst.ysG1u	149
; <u>-</u>	913		ATGATACAAGAATTATT	SAAGTTCTCTGTAAGAA	978
5	150	HisdluCysAsnIleAspGluValL	ysAsnValTyrPheLys	AsnPhelleProPheMet	169
ž	979	CALGAA DERAHINININININININININININININININININININ	AAAATGTTTATTTCAAA	AATTTTATACCTTTTATG	1038
40 dg	170	AsnSerLenGlyLeuValThrSerAsnGlyLeuProGluValGluAsnLeuSerLysArq 	snGlyLeuProGluVal	3luAsnLeuSerLysArg	189
i	3	Twee for the Leaf of the Conference			200
S S	5601	TYTOTTOTOTOTYTATOTYSASTOYSASTATOTYTTOTTOTTOTTOTTOTTOTTOTTOTTOTTOTTOTTO		LeuPheledAsphisAsp 	209 1158

do ob	210	LysThrLeuGlüThrAspSerlleAspSerPheGlüThrGlüAraThrProAraLysSer 	_ x
Oy Db	230	ASDIGUASPGIOGIAVATASBVATTIGPTOPTOHTS ThrPTOVATALGTBT GTBTVATMATASB 	æ
Qy Db	250	Thr HedinGinleuMetMetTleicuasnSeralaseraspdinProSerdiasnieu Hillifitii Hillifitii Hillifii ACTATCCAACAATTAATGATCTTTAAATTCAGCAAGTGATCAACGTTCAGAAAATCTG	<u> </u>
(ö. †	270 1339	ITESPTTyrTheAssAsnCysThrValAsnFroLysStatseLedeLydataValLys	_ æ
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Qy	330	LeuLysSerGluGluGluArqLeuSerfleGlnAsnPheSerLysLeuLeuAsnAspAsn 	_ ac
Oy Db	350		_ ∞
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Qy 10p	390 1699	LeuAsolesilysAlaPheAspPheTyrLysValileGluSerPheIleLysAluGluGly [1111] [111] [1111] [1111] [1111] [1111] [1111] [1111] [1111] [1111] [111] [111] [111] [11] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [111] [11] [111] [11] [111] [111] [11] [11] [111] [111] [111] [11] [11] [111] [111] [111] [11] [11] [111] [111] [111] [11] [11] [111] [111] [11]	_ ac
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Qy Db	450	GLYPTOThrAspHisLeuGlüSerAlaCySProLeuAshLeuProLeuGlüAshAshHis 	ac ac
Qy	470 1939	ThralaalaaspwettyricuserproValarysertychysiysiyselyserthrib 	_ œ
Oy au	490	ArgVaTASnScribtzATaAsnATaGTürbrGTürATaThr SetATaPheGTüTbrGTüTBTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	<u></u>
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oy Dp	530	ArglebashThriebCysGlbargleblebserGlbdhsproGlblebGlbdhis Helle 	_ œ
Oy Db	550	TrpfhrLeupheGluHisThrLeuGlnAshGluTyrGluLeuMetArgAsparqHisLeu 569 	30
ογ	570	AspGlnIleMetMetCysSerMetTyrGlyIleCysLysValLysAsafleAspLeuLys 589	-

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                                                                                                                                                                                  619 ArqValLeuIleLysGluGluGluTyrAspSerIleIleValPhcTyrAsnSerValPhe 529
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Retinoblastoma protein RB; K2F; transcription factor; human;
bladder cancer; restemosis; angioplasty; diabetic retinopathy;
thyreit hyperplasta; drave's disease; pseriagis;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  benian prostatic hypertrophy; Li-Fraumeni syndrome;
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This mucleotide sequence includes a coding region for relinoblastoma profer B & Gee ANWEASS). A new elabrael playpeptide to a tusion of: (i) a transcription factor (FF) comprising a DNA binding domain, and (ii) a retinoblastoma (FE) polypeptide that includes a growth suppression domain. Also new are: (i) a nucleic and encoding the lusion profein, and (2) expression vectors containing such DNA. The fusion protein, particularly expressed from gene therapy
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                439 ATOTGTATOTTTATTGCAGCAGTTGAGGTAGAGA IGTGGT FGAGTTTTAGTGAGGTA 498
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      199 (1999) North Contraction Contraction (1986) North 
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3.78
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  61 CysGlnLysLeuLysIleFroAspHisValArqGluArqAlaTrpLeuThrTrpCluLys HO
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        transcription of the E2F promoter than Rb alone and cause cell-cycle arrest in a variety of cells.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          1 MetProProLysThrProArgLysThrAlaAlaThrAlaAlaAlaAlaAlaAlaAla61@Pro 20
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      rectors (especially adenovirus vectors), is used to treat the bladder) or restructions, specifically cancer (particularly of the bladder) or restructions is (after adjust;), but also diabetic retinopathy, thyroid hyperplasia, Grave's disease, psoriasis, aniqu, prostalic hyperthospy, Li-Exammer, syndiams and peripheral vascular disease. Instance, protession of ESF-RB fusions is provided. The fusion proteins are more effective in repressing
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        New fusion polypeptide of, e.g. transcription factor - used to
treat, e.g. hyper-proliferative disease such as cancer and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Sequence 2994 RP; 974 A; 618 C; 593 G; 809 T; O other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Conservative:
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Example 1; Fig 2A; 91pp; English.
97WO-US21821
                                                                                97US-0801092
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                                                                                                                                                                                                          (CANJ-) CANJI INC.
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13-NOV-1997;
                                                                                14-PEB-1997;
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Tue Jan 21 10:04:13 2003

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011		110
* 13	CTCLLCAGGAAATTGGAAAGGACATGTGAAGTTATATATTTGAGACAAGCAGGTTGG	678
110		110
1,74	ATATCTACTGAAATAAATTCTGCATTGGTGCTAAAAGTTTCTTGGAGGATCACATTTTATTA	738
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1 4.4 /	ONTAAAOOOBAAGTATTACAAA LOGAAGATGT GGTGATTTTGATT LGAGTTAATGGTA	198
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6,6,7	TOTOTOTOTICANTATE LATTAAACTCTCACCTCCCATGTTGCTCAAAGAACCATATAAA	858
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170	ASBECTEGISTECUS THE SCEASINGLY CONTROL OF UVALCHUS ASBECT STATE AND THE HELLER	189 1098
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δ	370	SerThrSerGlnAsnLeuAspSerGlyThrAspLeuSerPheProTrp11eLeuAsuVa1	÷.
qq	1639	AGTACATCTCACATCTTCATTCTGCAACACATTCTCCCATCCAT	16.98
à g	390 1699	390 Leudsbloglysdlafbenspfbefyrlysvallledludserfbolledgafladlady 409 	409 1758
o रु	410	AsniculhrargGluMet iletysHistonGluarqCysGluHisArq1teMet GluSer 	424
ò	430	reconstruction and the control of th	449
q	1819	CTTGCATGGCTCTCAGATFCACCTTATTTGATTAAACAAFCAAFCAAACAACAAA	1878
y do	450	GlyProThrAspHisLeuGluSerAlaCysProLeuAsuLeuProLeuGluAsuAsnHis [111][11][11][11][11][11][11][11][11][1	4 6 4 8 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
ογ	470	ThralaalaaspMetTyrLeuSerProValArqSerProLysLysClyselTrilli	489
qq	1939	ACTGCAGAGATATGTTCTTCTCTCTGTAAGATCTCCAAAGAAAAAAGGTTCAACTACG	1538
Q O	490 1999	ArgVaTASBSETThrATaASBATAGTuThrGTbATATThrSerATatheGTbThrGTbTtyS 	503 2058
ò 6	510	ProLeuLysSerThrSerLeuSerLeuPhrTyrLysTysValTyrAtuLeuAlaTyrLeu 	529
o y	530	Argicularity toucygo the release of the sproduction	549
qq	2119	GGGTTAAATACATTTGFGAAGGCTTGTGTGTGTGTGTGTGTTTTTTTTTT	2178
9 Q	550	TrpThrLeuPheGluBisThrLeuGlnAsnGluTyrGluLeuMetArqAspArqBisLeu 	569
o,	570	AspGlDITeMetMetCysSerNetTyrClylleCystysValLysAsulleAspLentys	589
qq	2239	GACCAAAITATGATGIGITCCATGIATGGCAIAIGCAAAGGAAGGAAGAATATAAA	8677
Oy Dp	590 2299	Phetys Hellevalthralafyrlysasplæuptohtsalavalglmbluthrehetys 	609 2458
ολ	610	ArqValLeurlleLysGluGluGluTyrAspSer1le1leValPheTyrAsnSerValPhe	624
qq	2359	CONCINENTIGATICA A A GABAGA GA TATA A TATA TATA TATA TA	2418
5 8	630	MetalnArqtenLyaThrAsnIleLeadlnTyrAlaserThrArqProproftstorger The Control of the C	649
3 6	. 650	ALGGANDAGAR, INVANA MARTIA ILIGGANI ARIA ILIGGANG, MANGARING GARGARA GALIGARA Proli eprobis Il eprobrasce prolivilas Phebroses Serptolegala il lebro	2 7 7 7 3 3 4 4 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
qa	2479	CCAATACCTCACATCCTCGAAGCCCTTACAAGTTTCCTAGTTCACCTTACGATTCCT	2538
çò	670	61y61yAss11eTyr11eSerProLeuLysSerProTyrLysI1eSer61u61yLeuPro	689
qq	2539	GGAGGAACATCTATATTTCACCCCTGAAGAGTCCATATAAAATTTTAGAAGGTCTGTCA	7598
5 6	0690	ThrProThrLysMetThrProArqSerArqHeLeuValSerHedlyUsorPhedly ThrProThrLysMetThrProArqSerArqHeLeuValSerHedlyUsorPhedly ThrProThrProThrProArqSerArqHellHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	709
3 6	710	REPRESENTATION OF THE SAME OF	207
, d	2659	ACTCCGAGAAGTCCAGAAAATAAATCAGATGGTATGTAACAGGACGACGTGTGTCTAAA	2718

Sequence 2994 BP; 974 A; 618 C; 594 G; 808 T; 0 other;

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This sequence represents the wild type human retinoblastoma gene. The invention relates to a method of detecting a mutated retinoblastoma (with northic acid in mammals comprising hybridizing an isolated for itemath, wild type NB (with) TONA probe to a cell sample and detecting a mutated NB nucleic acid. The method is useful as a diagnostic
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  PR denot human; retinoblastoma denot mutation detection; immunoscreening; retinoblastoma diagnosis; hereditary retinoblastoma; secondary cancer; osteosarcoma; fibrosarcoma; glioblastoma; breast cancer;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      tool for diagnosing retinoblastoma. RB cDNA or genomic DNA are preferably used as probes to determine the defect region of the mRR gene through genomic DNA blotting analysis or using the method of restriction fragment length polymorphism analysis to determine the diseased allele. Cloned RB
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  cancer, such as, ostcosarcoma, fibrosarcoma, gliobiastoma, breast cancer, whether or now connected with residualisations. The method is plan used in the suppression of tumouniqueesis where the absent RB protein ppRRIIO will be provided through the molecular induction and genericansplanting of the RB cDNA to the individual in need of ppRBIIO.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  namilies with a history of boraditary relinchlasters and for acrossing their children. It may also be used in prophylactic and postnatal screening and for the prediction of the development of serondary
                                  2773 GSATCASATGAAAGCAGAAGGAAAGTAAAACATCTCCCASAGASAGTGTCCAAATTTCAGSAGAAAA 2838
                                                                                                                                                                                                                                                                                                                                                                          cDNA can be used to generate specific anti-RB protein (anti-ppRB110) antibodies which are useful for immunoserrening of tissue biopsy. The
7.1 Ard Ser Alag 1 uG 1 y Ser Asa ProProC y 3 ProCeaLy 5 Ly S Leu Arg Pho Asp 1 le G lu 749
                                                                                                                                                               740 @1ySerAspGluAlaAspGlySerLysHisLouProGlyGluSerLysPbeGluGlnLys 769
                                                                                                                                                                                                                                                                                                                               779 LouAlaGluMetThrSerThrArgThrArgMetGlnLysGlnLysMetAsnAspSerMet 789
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Will type human retinoblastoma gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            2844 GALACCICAAACAAGGAAGAGAAA 2922
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          740 AspIhrSerAsnLysGluGluLys 797
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                AAZ40287 standard; cDNA; 2994 BP.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     259 GACCIGCTOTOTOGGGTTGAAGAAAAAAAAAAAAAAAAAAAATTTTACTGCATTA 318
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                739 GYTAAAGGGGAAGTATTACAAATGGAAGATGATGTGGTSAITICAITICAGTTAATGCTA 798
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     21 ProAlaProProProProProProGluGluAspProGluGlnAspSerGlyProGlu 40
                                                                                                                                                                                                                                                                                                                                                                                                                                                     1 MetProProLysThrProArgiysThrAlaAlaThrAlaAlaAlaAlaAlaGluPro
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                                      550 TrpThrLeuPheGlnHisThrLeuGlnAsnGluTyrGluLeuMetArqAspArqHisLeu 569
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                                                                                                                                                                                                                                                            750 GlyScrAspGluAlaAspGlySerLysHisLeuProGlyGluSerLysPheGlnGlnHys
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Human pl10-RB retinoblastoma tumour suppressor encoding CDNA.
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adenovirus expression vector, where the vector has an insert of excaemous DNA comprising a gene encoding a foreign protein and adenovirus DNA in which all of the coding sequences of Ela, Elb, and protein IX, and part of SI are deleted, the vectors are useful in gene therapy treatment of cancer, especially for treating p53 deficient tuments. The excitences suffer and since efficient gene therapy of cancer. The present sequence encodes human p10-RB retinoblastoms tument suppressor which can be used as the foreign gene therapy of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     The present invention describes a composition comprising a recombinant
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Recombinant adenoviral vectors wasted for gene therapy of cancer, especially p53 delicient tumours
                                                                                                 /noter "retinoblastoma tumour suppressor"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Sequence 2995 BP; 975 A; 618 C; 593 G; 809 T; 0 other;
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/product- "pl10-RB"
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94US-0246006.
97US-0959638.
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28 Oct-1997;
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25 - NT - 1993;
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Óγ	110		110
QU	559 AG	FACCAAAGTTGATAATGTGAGAGTGTTGAGAABAAGTATGATGATGTTGTTGGTTTGG	618
OY	110		1
Dp	619 CT	TTTAGCAAATTGGAAAAGGACATGTGAACTIAIAIATTIGACAAACCAGCAGLOG	A. X.
ΟY	110		110
r q	679 AT	ATPOTAGAAATAAATTGTGGA PTGGTGCTAAAAGT TTGTTGGATCACATTTTTATTA	7 18
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i di	739 60	FAAAGGGGAAG FATT AGAAATGGAAGA LGATCTGGTGATTTCATTTTCAGTTAATGCTA	748
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ទី	474 E/A	DAABBITAATAIAGATGAGGFGAAAAAIGITIAIIITGAAAAATTTIAIACCITTTATG	÷ ⊝.
δō	170 Ası	nSerfeuGlyteuValThrSerAsnGlyteuProGluValGluAsnLeuSerTysArg	189
qu	1039 AA	FTP-FPTFTGGAPTTGTAAGATGTAATGGAGTTGCAGAGGTTGAAAATGTTTGTAAAGGA	367
;~	190 TY	rGluGluIleTyrLeuLysAspLeuAspAlaArqLeuPbeLeuAspHisAop	507
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qu	1219 AAC	POLITICAL GAAGA GOTGAAT GITAAT TOOTOO A GAAGA GOAGT TAGAACTOTALGAAC	1278
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qq	1279 AC	IATCCAACAATTAATGATGATTTTAAATTTAAGAAGTGATGAAGCTTCAGAAATCTG	1338
I_0	270 114	oSerfyrthcAsnAsnCysThrValAssProtysClaSerTloLcutysArqValtys	588
qq	1339 AT		365
οy	290 AS	p11eGlyfyr HepheLysGluLysPbeAlaLysAlaValClyClnGlyCysValGlu	309
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comprising a deletion in the protein IX gaue and a gene coronding a foreign protein. This vector can be used in gene thorapy, particularly to introduce tumour suppressor genes into cancerous cells. Genes which may suppressor quells, thymidine kinase and refinoblastoma tumour suppressor gene.
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               2779. GGAYCAGAAGGAGGAAGTAAAAGTAAAGGAGGAGGAGGAGGAGTYGAAATTLCAGYAGAAA 2838
                                                                                                                                                                                        730 ArqSerAlaCluGlySerAsnProProLysProLeulysLysLeuArqPheAsplleClu 749
                                                                                                               750 GlySerAspGluAlaAspGlySerLysHisLouProGlyGluSerLysPheGluGluLys 769
                                                                                                                                                                       770 LeualaGluMetThrSerThrArqThrArqMetGluLysGluLysMetAsuAspSerMet 789
710 ThrSerGluLysPheGlnLysIleAsuGlnMetValCysAsuSerAspArqValLeuLys 729
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  The present invention describes an adenoviral expression vector
                                                                                                                                                                                                                                                                                                                                                                                                                                Retinoblastoma; tumour suppressor protein; Rb; p53; cancer; adenoviral vector; gene therapy; thymidine Kinase; ds.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Sequence 2995 BP; 975 A; 618 C; 593 G; 809 T; 0 other;
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                                                                                                                                                                                                                              Disclosure; Fig 3; 49pp; English.
                                                                                                                                                                                                                                                                                                                  AAH25755 standard; DNA; 2995 BP.
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1279 ACTATCCAACAATTAATGATGTTTAAATTCAGCAAGTGATCAACCTTCAGAAAATGTG 1338
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                                                                                                                 230 AsnteuAspGluGluValAsnValIleProProHisThrProValArgThrValMetAsn 249
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expostatic, antithyroid, antipsentatic; adenoviral protein IX; psoriasis; thyroid hyperplasta; Crave's disease; hepatocellular carcinoma, neoplasm; benut prostatic hypertropky; il-Fraumen sycatome; sickle cell anaemia; lay Sachs disease; leukaemia; layphoma; adenovirus vector; cancer; ss.
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                                                                       570 AspellatioMotMctCysScrMctTyrGlylloCystysValLysAsnlleAspLeufys
                                                                                                                                                                                                                                                                                Retinoblastoma tumour suppressor protein, pllURB cDNA.
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The present cDNA sequence encodes retinoblastoma (RB) tumour suppressor protein, desidanted as p10RB.

Protein, desidanted as p10RB.

Characterised by the partial or total deletion of the adenovial protein IX DNA beginning at nucleotides (57 or 360 and ending at 1920 4050, and having a gene encoding a foreign protein such as tumour suppressor protein, F10RB (Feticoblaska) and F3 Adenovias we for is used for screening tumour suppressor quees useful in gene therapy. The vertor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             is particularly useful for treating or reducing hyperprolificative cell disorders such as thyroid hyperplasia, Grave's disease, psoriasis, benique prostatic hypertrophy. In Fraumeni syndrome, cancers specifically hepatocellular carcinoma, neoplasms, leukaemias, lymphomas, etc. to inhibit tumour prolifieration or to anteliorate particular related pathology such as sickle cell anaemia and Tay-Sachs disease. The vector
                                                                                                                                                                                                                                                                                                                                         New recombinant adenovirus expression vector having a gene encoding for a foreign protein and a partial or total deletion of the adenoviral protein IX DNA, useful in gene therapy for freating or reducing
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           is also useful for the safe recombinant production of diagnostic and therapeutic polypeptides and proteins.
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Methodiastoma; tumour suppressor protein; p130-KB; cell cycle; p53; Mb; mitosin; cell death; ademoviral protein LX; quee therapy; cytostatic; ademovirus expression vector; tumour; non-small cell lung cancer;
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melanoma; retinoblastoma, colorectal carcinoma; sarcoma; Wind's tumour;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Retinoblastoma tumour suppressor protein pll0 RB encoding cDNA.
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(WILLZ) WILLS R.N.
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The present invention describes a recombinant adequests systems to we vector, which comprises a partial or total deletion of a protein IX DNA and a quone encoding a foreign protein. The recombinant adequations wertor can be vectorstatic activity and be used in quone though, the recombinant adenovirus expression vector is particularly useful for treating the recombinant adenovirus expression vector is particularly useful for treating cancer, analy self lung cancer, analy self lung cancer, breatto a fumour, e.g. non small cell lung cancer, melanoma, retinoblastoma, breast tumour, colorectal carrinoma, sarroma, prostate tumour, bladder tumour, tumour of the reticulorablastoma, tissues, Wilm's tumour, astrocytoma diloblastoma, neuroblastoma, escondarian carcinoma, astrocytoma or renal cancer. The present sequence encodes the retinoblastoma tumour suppressor protein pl10-RB, which is
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2119 GGGTAAATAGAGTTTGTGAAGGCTTGTGTGTGAGGAGGAGGAATTAGAAGALALGA 2178
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                     2299 TTCAAAATCATTGTAACAGCATACAAGGATCTTCCTCATGCTGTTCAGGAGACATTCAAA 2358
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This sequence encodes a modified relinoblastoms tuned suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
                                                                                                                                                   Modified retinoblastoma tamour suppressor; KTSP profein; cancer therapy; cellular proliferation inhibitor; ss.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    inhibiting cellular proliferation, particularly cancer
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Mismatches:
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                                                                                       Modified retinoblastoma fumour suppressor gene.
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                              02 DEC 1998 (lirst entry)
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Best Local Similarity:
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ć	101	IleCysIlePheIleAlaAlaValAspLeu	110
qq	107	HTHTTTTTTTTTTTGCAGCAGTTGACCTAGGTGATATGTCATTTTTTTT	46.6
67	110		1.10
qq	167	CAGAAAAAACATAGAAATCAGTGCCATAAATTCTTTAACTTACTAAAAGAAATTGATACC	426
ς	110		110
d d	427	AGTACCAAAGTIGATAATGCIATGTCAAGACTOTIGAAGAAGIATGATGTTGCA	486
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qu	487	CTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATATTGACAACCAAC	546
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qq	547	ATATCTACTGAAATAAATTCTGCATTGGTGCTAAAAGTTTCTTGGATCACATTTTTATTA	606
οy	110		
qq	607	GCTAAAGGGGAAGTATTACAAATGGAAGATGATCTGGTGATTTCALTTCAGTTAATGCTA	999
ολ	. 110		110
qq	667	TGTGTCCTTGACTATTTTAAACTCTCACTCTCCATGTTGTTCAAAGAACATATAAAA	726
ò	111	AlaVall1eProlleAsm31ySerProArqThrProArqArq61yG1nAsmArqSer	129
qa	727	ACAGGTGTTATACCCATTAATGGTTCACCTCGAACACCCAGGCGAGGTCAGAACACGGT	786
Š í	130	130 AiaArqileAiaiysGlnieuGluAshAspthrArqiletieGluValleueysLysGlu 149	14.9
a S	/8/	GCACGGATAGCAAAACTAGTAGAAATGATACAAGAATTATTGAAGTTCTCTGTAAAGAA	846
λo i	150	HisGluCysAsnIleAspGluValLysAsnValTyrPheLysAsnPheIleProPheMet	169
a a	94/	CATGAATGTAATATAGATGAAGAGTGAAAAATGTTTGAAAAATTTTATAG	906
à á	1/0	AshSerLend(JyLenValThrSerAshGlyLeuProdLuValGluAshLeuSerLysArd - -	189
à	50	THE CLUSTER AND ARREST OF THE CHARLES OF THE CONTROL OF THE CONTROL OF THE CLUSTER OF THE CLUSTE	9 3
S 3	561		1036
ŝ	210	LysThrLeuGlaThrAspSer11eAspSerPheGlaThrGlaArqThrProAralysSer	523
QCI	1027		1086
ò	230	AsnLeuAspGluGluValAsnVallleProProiisThrProValArqThrValMetAsn	543
qa.	1087	ACCTIGATGAAGAGGGAAGGAATTGCCCCCACACACACTCAGTTAGAACTGTTATGAAC	1146
О.	250	Thr Legingin Leuwet Met ille Leus in Ser Alaser Aspdin Proser GloAsideo	269
qq	1147	ACTATCCAACAATTAATGATGATTTTAAATTCAGCAAGTGATCAACCTTCAGAAAAATCTG	1206
οχ	270	IleSerTyrPheAsaAsaCysThrValAsnProLysGlaSerTleLeutysAraValLys 	587
Q.	1207	ATITICCTATITI TAACAACTIGCACAGTIGAATCCAAAAGAAAGTATAGTIGAAAATAGTIGAAGT	1260
à à	1267	AspiledlytyrilePheLyschuLysReAldrysAldValdtychnGlycysValdtu 	904
à		CHARLES CONTROLLES AND	7.1
<u>7</u> 2	1327	1957 2567 5 1847 1717 2588 2685 2784 1847 2785 2785 2785 2785 2785 2785 2785 2 1877 2785 1877 2785 2	529 1386

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This sequence encodes a modified retinoblastoma tumour suppressor protein (RISP) of the invention. The proteins can be used for inhibiting regular prolliteration, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular prolliferation, particularly cancers. The RISPs have a broader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Modified retinoblastema tomour suppressor: BTSP protein; cancer therapy; cellular proliferation inhibitor; ss.
                                                                                                                                                          2527 ACTICTGAGAAGTTCCAGAAAATAAATCAGATGGIATGTAACAGCGACGGTGTGCTCAAA 2586
                                                                                                                                                                                                                                                                                                                                                                                                        2647 GGATCAGATGAAAGTAGAAGTAAACATCTCCCAGGAGAGTCCAAATTTCAGCAGAAA 2706
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                                                                                                                                                                                                                                                                                                                                           730 ArgSerAlaGluGlySerAsnProProLysProLeuLysLysLeuArgPheAspIleGlu 749
                                                                                                710 ThrSerGluiysPheGlniysIleAsnClnMctValCysAsnScrAspArgValLcuiys 729
      2467 ACACCAACAAAAAGACICCAAGAICAAAAAAICIIAGIACAAIIGAIGAAICAIIGGG
                                                                                                                                                                                                                                                                                 2587 AGAAGTGPTGAAGGAAGPAAGGPTPPTTAAAGGACTGAAAAAGTAGGTTTTGALALIGAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                  770 LeuAlaGluMetThrSerThrArgThrArgMetGlnLysGlnLysMetAshAspSerMet
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                                                                                                                                                                                    .447 AITITICAIAIGTETTTATTGGCGTGCCCTCTTGAGGTTGTAATGGCCACATATATGGAG
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                                                                                                                                                                                                                                                                                                                                                                        LeuAsnLeuLysAlaPheAspFheTyrLysVallleGluSerFheIleLysAlaGluGly 409
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*** LeuLysserGluGluArgLeuSerIleGlnAsnPheSerLysLeuLeuAsnAspAsn 349
                                                                                                                             45. (LephchisMetSerLeuLeuAlaCysAlaLeuGluValValMetAlaThrTyrSerArg 369
                                                                                                                                                                                                                                                    (2) SetThrSetGInAsnLeuAspSetGlyThrAspLeuSerPheProTrp11eLeuAsnVal 389
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      430 LouAlaTrpLeuSerAspSerProLeuPheAspLeuIleLysGlnSerLysAspArgGlu 449
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Pred. B Score: Bercent Best La Query B		: imilarity: I Similarity: ch:	0 4068.50 85.88% 85.88% 98.18%	Length: Matches: Conservative: Mismatches: Indels: Gaps:	3555 797 0 0 0 131 1	
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oy	210	LysThrieuGinthrAspSertleAspSertPeGluthrGinArgthrProatalysSer	229
Db			1086
Oy	230	ASILGUASPGTUGTUVATASINVATTTOPTOPTOHTSTHTPTOVATAIGTUTVATMICTASIL	249
Db		TELETETTTOPTOAGGGGGGAATGTAATTGCTCCACACTCTAGTTAGGACTGTTAGAAC	1146
Qy	250	ThrileGinGluLeuMetMetTleLeuAsnSerAlaSerAspGluProSerGluAsnLeu	269
Dp			1206
O _y	270 1207		289 1266
Qy	290	ASPITECTYTTICPESSCIULYSPECALALYSALAVATOTYTECTYTETTICTTTTTTTTTTTTTTTTTTTTTTTTTTT	309
Db	1267		1326
δο do	310	IleGlyserGlnarqTyrLysLeuGlyValarqLeuTyrTyrarqvalMetGlaserMet 	1386
dd	330	LeulysSerGluGluGluArgleuSerffeGlnAsnPheserLysLeulsnasnAspAsn	349
	1387		1446
φο	350	TePheHisMetSerLeulcuAlaCysAlaLeuGluValValMetAlalhrTytSerArg	369
			1506
yo	370	SerThrSerGlnAsnLeuAspSerGlyThiAspLeuSerPheProTrpTelenenAsnVal	389
o	1507		1566
Oy	390	LeuAsnicutysAlaPheAspPhetyTiysValifeGinserPheffelysAladinGly [[HH]] [HH] [HH] [HH] [HH] [HH] [HH] [409
Db	1567		1626
Ογ	410	Asnieuthranglumetiletyshistoudiuaratyssiuhisaratiometdiuser 	424 1686
c cy	430	439 LeuNatrpLeuSerAspserProLeuPheAspLeuTleLyssinSerLysAspaugiu 449 	449 1746
QY Db	450	GLYPTOThTASPHISLOUGHUSOTALACYSPTOLOUGHENDLOUDHOLDUSHASHHIS HILLIH	469 1806
Oy	470	ThrataalaaspwetTyrLeuSerProVaTarqSerProLysLysLysGTysCThrift	489
Db			1866
c c	490	ArqVa1AsnSerThrAlaAsuAlaGluThrGluAlaThrSerAlaPheGluThrGluLys [11] [1]	509 1926
Oy	510	ProleulysSerThrSerLeuSerLeunhefyrLysLysVallyrArabeualafyrlau	529
Db	1927		1986
Oy Db	530	ArqLeuAsnThrLeuCysGluArqLeuLeuSerGluHisProGluLeuGluHis Helle 	549
ςò	550	TrpThrLeuPheGlnHisThrLeuGlnAsmGluTyrGluLeuMetArqAspArqHisLeu	569

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2047 T3GACCCTTTTCCAGCACACACCTGCAGAATGAGTATGAACTFATGAGACACAGGCATTTG 2106
                                                                                                                                                                      210.7 GACCAAATTATGATGTCTTCCATGTATGGCATATGCAAAGTGAAGAATATAGACCTTAAA 2166
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      222 CGIGITIIGALCAAAGAAGAGAGATATATATATATATATATATAAATTOTAAAAAAGTOLUG 2285
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                                                                                     5% AspOntioMotMotCysSerMotTyrGlytLoCysLysValLysAsnTloAspLauLys 589
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tetracycline repressor protein: TRP; tetracycline operator;
production; stable cell line, protein production:
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The present sequence appears in the specification, which describes a sequence encoding a Lusion protein comprision a transcriptional responsive expression vector (TREV), which contains a sequence encoding a Lusion protein comprision a transcriptional ransactivation domain (TTE) preservely attached to a tetracycline refressor protein (TRE), the first sequence operatively positioned downstream of a promoter. The vector also contains a cloning site operatory prestricts and absent produce stable cell retracycline perfector. The TREVS can be used to produce stable cell lines in which gene expression is tightly restricted by tetracycline. They can be used for the production of proteins such as tumour suppression provides which can be used for the production of proteins such as tumour suppression because the production of proteins such as tumour suppression provides.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  by abnormal cellular proliferation, particularly cancers.
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Best Local Similarity:
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	390	LeuAsniculysAlaPheAspPheIyTtysVallTeGluSerPheTteTysAlaGludIy 	409
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ς	430	LeuAlaTrpLeuSerAspSerProLeuPheAspLeuTleLysGluSerLysAspArqdlu	. 4
q	1687	CTTCCATGCTCTCACATTCACCTTATTCATCTTATTTATT	746
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qq	1807	ACTIGCAGCAGATATGTATCT FLCTCCTGTAAGATCTCCAAAGAAAAGTTCAACTACG	9.58
ζŅ	490	ArqValAsnSerThrAlaAsnAladluThrGluAlaThrSerAlaPhedluThrGluLys	5.0
00	1867	CGFGTAAATTCFAGTGCAAATGCAGAGAAAAAAAAAAGCTTGCAGATTCAGAAG	976
ΟŊ	510	ProLeulysSerThr SerLeuSerLeubhe lyr LystysVal lyr Ar dizeskia tyr len	5.7
qq	1927	COATGAAATCTACCTCTTTCACTGTTTATAAAAAGTGTATCGGCTAGCCTATCTC	986
δ	5.40	ArgicuAsnThricuCysGluArgicuLenSerGluBisProGluLeuGluBisHelle	٠ ۲
Q.	1987	CGGCTAAATACACT LIGTGAACGCCTTCTGTCTGAGCAGGCCAGAATTAGAATATATAT	046
δλ	550	TrpThrLeuPheGhillisThrLeuGhnAsnGluTyrGluLeuMetArgAspArgHisLeu	69
a C	2047	TOGACOCTITICCACCACACACTGCAGAATGAGTA IGAACTCATCACACACACAATTG	901
QY	570	AspGln11cMctMctGysGcrMctTyrGly11cOystysVallysAsm11cAspLcutys	5.8
qq	2107	GACCAAATTATGATGTGCATGTATGSCA1A1GCAAAG1GAAGAATATATGAAAAA	166
λo :	0.56	PhotystletlevalPhralatyttysAsplouProfitsAlaValOthotherphotys	5.0
90	2167	TITCAAAATGATTGTAACAGGATACAAGGATCT TGCTCATGCTTGAGGAGACATTGAA	477
ζλ	610	ArqValLeu1leLySGluGluGluTyrAspSor11e1leValPheTyrAsnSorValPhe	6.7
100	2227	CGTGTTTTGATCAAAGAAGAGGATATGATTCTALTATAGTATTCTATAAACTCTGTTCTTC	987
ς	630	MetGinArqueulys thi Asni JeleuGini yi AlaSer thi Arqproprothi Leusor	₹
qq	2287	ATGCAGAGACTGAAAAAATATTTTGCAGTATGCTTCCACCAGGCCCCCLACCTGTCA	446
Оу	650	Pro11ePro41s11eProArdSerPro1y1.1ysPheProSerSerPro1edArd.1ePro	5.9
qq	2347	CCAATACCTCACATTCCTCCAAGCCCTTACAAGTTTCCTAGTTCACCCTTACGAATTCCT	406
δλ	670	GlyGlyAsnlleTyrIleSerProLeuLysSerProTyrLysIleSerGluGlyLeuPro	б я
q	2407	GGAGGGAACATCTATTTTCACCCCTGAAGACTCTALATAAATTTTCAGAGGTTTTCAC	46.6
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qq	2467	ACACCAACAAAAATGACTCCAAGATCAAGAATCTTAGTATCAATTGGTGAATCATTCGGG	975
ολ	710	ThrSerClulysPheGlulys1!cAsnCluMetValOysAsnSerAspArqValLendys	ž,
£	2527	ACTTCTGAGAAGTTCCAGAAATAAATCAGATGGTATGTAACAGGACCGTGTGTCAAA	Ç E
ò	7.40	${\bf ArgSerAlaGluGlySerAsnProProLysProLevLysLysLysLeuArgPheAspI} \\ eGLucklysLysLysLeuArgPheAspI \\ eGLucklysLysLysLysLysLysLysLysLysLysLysLysLysLy$	2.

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DESIL: telomerase, catalytic subusit, reverse transcriptase, life span, of inclinations, p53, tumout suppressor, inhibitor, arterioseletosis, proliferation; immortal; tumour therapy; macular degeneration; activator;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     The invention concerns methods and reagents for extending the life-span,
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         comprises administering agents reversibly and ivating telemetase activity and reversibly inactivating Rb/INK4 and/or p53 pathways useful in treating age related diseases
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 include c4k4 or c4k6 mutants. In particular, a c4k4 mutant is one which differs from at one or more of residues K22, 924 H45 and/or P47 Additional constructs include a papilloma virus E7 protein, or other
                                                                                                                                                                     2647 GGATCAGATGAAGGAGGFGGAAGTAAAGTAGAGATGGAGAGTTTCAGCAAAA 2706
                                                                                                                                            23.4 LeuAlaGluMetThrSerThrArqThrArqMetGlnLysGlnLysMetAsnAspSerMet 789
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and arteriosclerosis. The cells can also be used to replace tunnour cell
lines in vitro and for studies on biochemical and physiological aspects
of growth and differentiation. Forgetting tived (immortal) cells could also be
of use in the production of normal or genetically engineered
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Rb; androgenic; antiandrowenic, identification; prostate cancer; ss.
                                                                                                                     550 TrpThrLeuPheGlnHisThrLeuGlnAsnGluTyrGluLeuMetArgAspArgHisLeu
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present invention can be used in screening assays to identify candidate pharmaceutical melecules for the ability to promote or inhibit the interaction of androgen receptors and androgen responsive elements to modulate androgenic eclivity. The identification and characterisation of androgen receptor co-activity as such as those of the invention will tacilitate the development of screening assays to evaluate the potential efficacy of drugs in the treatment of prostate cancer.
                                                                                                                                                                                                                                                                                                                                                                     Now) andrower receptor associated proteins used to detect androgenic of antiandrowenic activity in screening assays for candidate parameterical molecules which promote or inhibit the activity .
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Human retinoblasto Breast cancer rela Human retinoblasto Modified retinobla Modified retinobla DNA sequence of th Human androgen rec Modified retinobla Modified retinobla Description SUMMARIES AAV58440 AAV54990 AAV58450 AAV58452 AAU70536 AAA29391 AAZ88444 ABE62874 AAV58451 Onery Match Length DB 48.89 4597 4H 1.3 48.49 1554 3558 100.0 Score 1117 3183.6 3183.6 \$182.5 \$182.5 \$182.5 \$180.4 4169 ¥ 5, 1, J 4 Kersu] t

Hu S, Xu H, Zhou Y;

Benedict WF,

(BAYU) BAYLOR COLLEGE MEDICINE

20-FEB 1997;

(TEXA) UNIV TEXAS SYSTEM

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ALIGNMENTS

Modified retinoblastoma tambour suppressor, ATSP protein, caser therapy; cellular proliferation inhibitor; ss. Modified retinoblastoma tumour suppressor dene. Location/Qualifiers 7..2616 AAV58450 standard; DNA; 3377 BP. 47US-0038118. 98WO-US03041 02-DEC-1998 (first entry) /*tag- a 19-FEB-1998; HOMO Sapiens W09847091-A2 27-AUG-1998. AAV58450; RESULT AAV58450 SOU

0; profein (RTSP) of the invention. The proteins can be used for inhibiting relidiar profileration, when condministered with a p53 profein. The RTSPs can be used for treating diseases characterised by abnormal cellular. proliferation, particularly cancers. The RTSPs have a broader spectrum of activity than wild type RISPs. 12] CHGGGGAACHGGCTCTCTAGGHIGAGTTTGAAAAAAAAAAAAAAACHGATTTACT 180 12) CAGGAGGACTIGCCTCTGGICAGGCTTGAGTTTGAAGAACAGAAGCTGATTTTAGT 180 18.1 HINTITATHITONAAAATTAAAGATACAHATCATGAGAGAGAGAGGAGTTGGTTGG 240 24] GAGAAAGTI FCATCTGPGGAPGCAGPATTGGGAGGTVATATAAAAAAAAAAAAGAAGTG 300 LOGGGAALFIGIATETAFTERAGRERAGTEGACTEAGAFGACATGTCGTTCACTETACTE 360 38) IGGGGAA ICTGTATOTTTAT IGCAGCAGTTGACCTAGAFGAGATGTGTGGTGACTTAGT 360 361 GAGTIACAGAAAAACATAGAAATCAGTGTCCATAAATTCTTTAACTTAAAAAATT 420 36.1 GAGCTACAGAAAAAATAGAATCAGTGTCCATAAATTCTTTAACTTACTAAAAGAAATT 420 42: GATACCASTACCAAAGTTGATAALGCTATGTCAAGAGTGTTGAAGAAGTATGATGTTGTTG 480 421 GATACCAGTACCAAAGTTGATAATGCTATGTCAAGACGTGTGAAGAAGTATGATGTTG 480 48] HIGGACTOLICAGGAAAFTGGAAAAGGACATGTGAAATTTTGACACAGCAGC 540 541 AGTICGATGGTGGCTGTTAIACCCATTAATGGTCACCTCGAACACCAAGAGAGTGAG 600 Gaps This sequence encodes a modified relimbhastoma tumour suppressor 100.0%; Score 3377; DB 19; Length 3377; ., Retinoblastoma suppressor protein with N-terminal modification Indels Sequence 3377 BP; 1113 A; 654 C; 626 G; 984 I; 0 other; innibiting cellular proliteration, particularly cancer í, 0; Mismatches Pred. No. 0: iaim 22; Page 210-215; 249pp; English 100.08: Conservative Local Similarity WPI; 1998-480788/41. P PSDB; AAW69374. Matches 3377; Ouery Match

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781 TCTPAAACGATACGAAGAAATTTFATCTTAAAAATAAAGATCTAGATGCAAGATTATTTTG 840
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2941 A	AGGCTGTCTGACTTTGCCTTTTGTAGCATATAGGTGTTTGCTTTGTTTTTTTT	3000

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This sequence encodes a modilied retinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting
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                                                                                                                                                                                                                                                                                                                                              8061 TCTATCTTCCAAATGCAATTTGATTGACTGCCCATTCACGAAAATTATCCTGAACTCTTC 3120
                                             Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Modified retinoblastoma tumour suppressor gene.
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collular proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISFs have a broader spectrum of

-+ 12) CCGGAGGACTIGCCTCTCGTCAGGCTFFGAGTTTTGAAGAAACAGAAGCAGATTTFTACT 180 121 COGGAGGACTECTETETETAGGITEGAGTTTGAAGAAAGAAAAAAAACTEGATTTAGT 180 181 GCATTATGTCASAAATTAAAGATACCAGATCATGTCAGAGAGAGAGGGGTTAACTTGG 240 241 GAGAAAGTIICAIGIGGANGGAIATGGGGGTIATATATAAAAAAAAAAAGAAAGIG 300 141 GAGAAAGTIICATCIGIGGATGGAGTATTIGGAGGTTATATTCAAAAGAAAAAGGAACTG 300 361 GAGCIACAGAAAAACATAGAAATCAGTCTCCATAAATTCTTTAACTTACTAAAAAATT 420 481 IFTGCACTICTTCAGCAAATFGGAAAGGACATGTGAACTTATATATTTGACAACGCAGC 540 HITTGTATTTTCAAAAFDAAAAAAAAAAAAAAAAAATTATATATTTGAAAACGCAGC 540 361 GAGCTACAGAAAAACATAGAAATCAGTGTCCATAAATTCTTTAACTTACTAAAAGAAATT 420 421 GATACCAGTACCAAAGTTGATAATGCTATGTCAAGACTGTTGAAGAAGTATGATGTATTG 480 541 ACTICCATATCTGGAAATAAATTCTGCATTGGTGCTAAAAGTTTCTTGGALCACATTT 600 661 ATGCTATGTGTCCTGACTATTTATTAAACTCTCACCTCCCATGTTGCTCAAAGAAGAACCA 720 721 TATAAAACAGCTGTTATACCCATTAATGGTTCACCTCGAACACCCAGGCGAGGLCAGAAC 780 604 ASSACTOCTOSTANTAN TAAANTAASTA SAAATOATAATAATAATAATAA SAASAASTA SAASTATTATTATTATTATTATTATTATTATTA 663 781 AGGAGTGCACGGATACCAAAACAACTAGAAAATGATACAAGAATTATTGAAGTTCTCTGT 840 664 AAAGAACATGAATGTAATATAGATGGGGGGGAAAAATGTTTATTTCAAAAATTTTATACCT 723 841 AAAGAACAIGAATGIAATAIAGAIGAGGIGAAAAAIGIITAJITICAAAAAITITAIACCI 900 724 LITTATGAALICTCTTGGACTTGTAACATCTAATGGACTTCCAGAGGTTGAAAATCTTTGT 783 4; Indels 177; Gaps 1 CGCGTCATGCCGCCCAAAACCCCCCGAAAAAGGGCCGCCACCGCCGCGCGCTGCCGCCGCCGCG 60 94.3%, Score 3183.6, DB 19, Length 3555, 94 9%; Pred No. 0; Sequence 3555 BP; 1171 A; 684 C; 653 G; 1047 T; 0 other; 0; Mismatches activity than wild type RTSPs. Conservative local similarity 541 AGTICGAI----Matches 3373; Ouery Match 575 5888**%**% ć ä 9 ò Š 3 3 9 ò 3 5 ŝ 3 Š 3 5 8 S = 3 S ŝ 3 Š 2 ें 9 ŝ

964 ATGAACACTATCCAACAATTAATGATTTTAAATTCAGGAAGTGATGAACTTCAGAA 1023 1141 ATGAACACIATCWAACAATTAATGATTTTAAATTO'AGGAAGTGATGAOOTTO'AGAA 1200 1084 GIGAAGGAIATAAGATACAICITIAAAGAGAAATITGCTAAAGCTGGGGACAGGGTIGT 1143 1321 GIGGAAAIIGGAITACAADGATAGAAATIGGAAGTIGATIGATATAGAAGTAAGAAA 1380 1204 TCCATGCTTAAATCAGAAGAAGGATTATCCATTCAAAATTTTAGCAAACTTCTGAAT 1263 1381 TCCATGCTTAAATCAGAAGAAGAATTATGCATTCAAAATTTTAGGAAACTTCTGAAT 1440 1081 AAAAGTAACCIIGAIGAAGAGGIGAAIGTAAHICCIGCAGAGACIGCGGITAGGACIGII 1140 1144 GTGGAAATTGGAGGGGGGAACAAGTTGGAGGTTGGTGGGTATAGGGGAGIAATGGAA 1203 1441 GACAACATTTTTCATATGTCTTTTTGGCGTGGGTTGTTGAGGTTGTAATGGCCACATAT 1500 1324 AGCAGAAGTACATCTCAGAATCTTGATTCTGGAACAGATTTGTCTTTCCCATGGATTCTG 1383 1384 AATGTGCTTAATTTAAAAGCCTTTGATTTTTACAAAGTGALCGAAAGTTTTATCAAAGCA 1443 1681 GAATCCCTTGTATGGCTCTCAGATTCACTTTATTTGATCTTATTAAACAATCAAAGGAC 1740 1804 TATCTCCGGCTAAATACACTTTGTGAACGCCTTGTGTGAGCACCCAGAATTAGAACAT 1863 1021 CATGATAAAACTCTTCAGACTGATTCTATAGACAGTTTTGAAACACAGAGAACACCACAGA 1680 CAGAAGCCATTGAAATCTACCTCTTTCACTGTTTTATAAAAAAGTGTATCGGCTAGCC 1803 1921 CAGAAGOOATTGAAATOTAOOOTOTTTTGAOTGTTTTATAAAAAAGTGTATGGGGTAGGC 1980 901 TITALGAALICICITIGGACTIGIAACAICTAAIGGACTICCAGAGGTIGAAAAICTTICT 960 784 AAACGATACGAAGAAAIITATCITAAAAAIAAAAGATCIAGAAGATTATTTTGGAT 843 904 AAAAGTAACGTGAAGAAGGGAATGTAATTCCTCCACACACTCCAGTTAGGACTGTT 1561 AATGTGCTTAATTTAAAAGCCTTTGATTTTTACAAAGTGATGGAAAGTTTTATCAAAGGA GAAGGCAACTTGACAAGAAAATGATAAAAACATTTAGAACGATGTGAACATCGAATCATG 1504 GAAICCHIGGAFGGFICIGAGAFICAGHITAFITIGAICHFAFIAAAGAAFCAAAGGAC 1684 ACTACGGGTGTAAATTCTACTGCAAATGCAGGACACAAGGAACAAGCAACCTCAGAGC 1264 GACAACATTTTCATATGTCTTTATTGGGGTGGTGGTTTTGAGGTTGTAATGGGCACATAT 1564 CGAGAAGGACCAACTGATCACCTTGAATCTGCTTGTTGTTCAATCTTGCTCTCCCGACAAT 1744 1444 .δ <u>م</u> q ŝ ò pp Š 5 g qq δ a 끕 g g a Ωp ΣÞ da, QQ qq οğ Š οy ò Οy 금 ŏ ò ŏ

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ATCATCTIGGACCTTTTCCACTCTGGAGAATGAGTATGAGCTCATGAGAGGAGG TTTTTTTTTT	AAATTCAAAATCATTGTAACAGCATACAAGGACTTCCTCATGCTGTTCAGGAGACAAAATTCATTTTTTTT	GPCTTCALGCAGAGACTGAAAAAAATTTTGCAGTATGCTTCCACCAGGCCCCCTACC CHTILLILLILLILLILLILLILLILLILLILLILLILLILL	TCACCCC1GA 1111111111 1CACCC1GA CCAAGA1CAA 111111111	TTGBBBCTFCTGAGAAGTEGGGAAAATAAATGGGTTGGTAACAGGGACGGTGTG HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	ATTGAAGGATCAGATGAAGCAGATGAAGTAACATCTCCCAGGAGAGTCCAAATTTGAGGATTGAAGGATGAAAGTTTTGAGGATGAAGGATCAGAATTTTGAGGATGAAGGATCAGAAGGAGAGTCCAAATTTTGAGGATTGAAGGATTGAAGGATTTTGAAGAAATTTTGAGGAAAACTGAAAAGAAAATTTTGAGAAAACTGAAAAAGAAAAAGAAAAATTTTAAGAAAAAGAAAAAGAAAAAGAAAAAGAAAAAGAAAAAGAAAA	MACATGRAFACTICAAACAAGAAGAAATGAGGALCTCAGGACCTTGGTGACACTGT 28 LITHTHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	TTATGGCAVATTTAATATCTTCAGCTCTTTTTGGGATATAAAATGTGCAGATGCAATT HHILLHIHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	APTICIO I AAATCC DOCCATTIAAAAGTTO I AGGACATTG PITTO PCTTC CAAAGTAA ALT LOTELLI HILLI
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                                                                                                                                                           3301 AAAAATGGATATTATTAGAAATTAGAAAAAAATTACIAATTTACACATTAGATTTATT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Minimal promoter, tetracycline responsive expression vector; IREV;
                                                                                                                                           3124 AAAAATGGATATTATTAGAAATTAGAAAAATTACTAATTITIACAATTTAGATTTTATT
                                                                                                                                                                                                   3064 ATCTTCCAAATGCAATTTGATTGACTGCCCATTCACCAAAAATTATCCTGAACTCTTCTTCTGC
                                                                                                                                                                                                                                      8244 NANAGCIGGAAGCAAAGIATAACCATAIGAIACTAICATACTACTAAAACAAATITCAIA
                                               3004 TAATTTATATGTATTTTTTTAATTTAACATGAACACCCCTTAGAAAATGTGTCCCTAGC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   tightly controlled expression of genes, such as tumour suppressor genes for treating cancers
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           transcriptional transactivation domain; TTD;
tetracycline repressor protein; TRP; tetracycline operator;
production; stable cell line; protein production;
tumour suppressor protein; treatment; cancer; ss.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         DNA sequence of the specification.
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The present sequence appears in the specification, which describes a tetracycline responsive expression vector (TREM), which describes a tetracycline responsive expression vector (TREM), which contains a sequence encoding a fusion protein comprising a transcriptional transactivition domain (TD) operatively attached to a tetracycline repressor protein (TRP), the lins sequence operatively positioned downstream of a basal promoter comprising a tetracycline operator. The vector also contains a cloning site operatively positioned downstream of a basal promoter comprising a tetracycline operator. The TREWs can be used to produce stable cell lines in which gene expression is tightly requiated by tetracycline. They can be used for the production of proteins such as tumour suppressor proteins which can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers.

Superior 3555 BP, 1171 A, 684 C, 653 G, 1047 T, 0 other,

Query Match Best Yord Cimilarity 94 0%; Prod No A; Matches 3373; Conservative O: Mismatches 4; Indels 177; Gaps

549 · · · · · - GGT/GGTGT/ATACCCAT/AATGGT/CACCT/CGAACACCCAGGCGAGGT/CAGAAC 603 241 GAGAAAGTIFGATOTOGATGGAGTATTGGGAGGTTATATTGAAAAAGGAAAGGAACTG 300 TGGGGAATCTGTATTTTATTGCAGCAGTGGAGTGAGATGAGATGTGGTTTTACT 360 (4.1. GAGCTACASAAAAACATAGAAATCAGTGTCCATAAATTCTTTAACTTACTAAAAGAAATT 420 4.21 SATACCAGTACCAAAGTIGATAATGCTATGTCAAGACTGTTGAAGAAGTATGTATTG 480 660 FIATIAGGIAAAGGGAAGGTAFTAGAAGAGAGATGATGGTGGTGGTFTGGTFTGGTFTA 660 651 ATGCTALGTGTGTCCTTGACTATTTAAACTCTCACCTCCCATGTTGCTCAAGAACCA 720 541 AGTTCGAIAICIACIGAAAIAAAIICIGCAIIGGIGCIAAAAGIIICTIGGAICACAITT 600 541 AGETGGAT--------- 615 5 Ξ 5 ŝ ŝ 5 12 3 $\frac{2}{5}$ ê 5 5 <u>2</u> 3 Š

21 TATAAAAYAGUGTATTATAAAAATGGTTCAACCTGGAACAACAGGAGGGGAGAAAA 780

1081 AAAAGTAACCTTGATGAAGAGGAALGIAALLCCTCCACACACCCAGTAGGACTGIT 1140 964 ATGAACACTATCCAACAATTAATGATGATTTTAAATTCAGCAAGTGATCAACCTTCAGAA 1023 1084 CTGAAGGATATAGGATACATCTTTAAAGAGAATTTGGTAAAAGGTGTGGGGGGGTGT 1143 1144 GTCGAAATTGGATCACAGCGATACAACTTGGAGTTGGCTATGTATTACCGAGTAATGGAA 1203 1204 TCCATGCTTAAATCAGAAGAAGGATTATCCATTCAAAATTTTAGCAAACTTCTGAAT 1263 1381 ICCAIGCTTAAATCAGAAGAAGAACGATTATCCAITCAAAATTTTAGCAAACTICTGAAT 1440 1264 GACAACATTTTTCATATGTGTTTTTGGGGTGTGTGTTTTTGAGGTTGTAATGGCCACATAL 1323 1324 AGCAGAAGTACATCTCAGAATCTIGALICTGGAACAGALLIGICTTICCCALGGALLCIG 1883 1501 AGCAGAAGPACAPCPFAAAPCPFAATAGATFFTGGAAGAGATFFTGPCPPTGCCAPGGAFTCTG 1560 1384 AAIGIGCIIAAAIIIAAAAGCCIIIGAIIIIIACAAAGIGAICGAAAGIIIITAICAAAGCA 1443 1621 GAAGGCAACTIGACAAGAAAAGATAAAAACATITAGAACGATGIGAACATCGAATCAIG 1680 1504 GAATUUCITGUATGUTUTUAGAITUAUNITTAITIGATUTTATTAAAUAATUAAAGGAU 1563 1564 CGAGAGAGATTGATCACCTTGATCTGCTGCTGTTAATCTTCTGCTCTGTAATCTTCTGAAATCTGCAGAAT 1623 1624 ANYCACACTGCAGGAGATATGTATGTTTCTCCTGTAAGATGTCCCAAAAAAGAAAAAAGTTCA 1483 1444 GAAGGCAACTI'IGACAAGAAAATGATAAAAGATTTAGAAGGTGTGTGAAFATGGAATGATG 724 TTTATGAATT-CTCTTGGAGTTGTAACALCTAALGGAGTTGCAGAGGTTGAAALGTTTCT 783 784 AAACGATACGAAGAAATTTATCTTAAAAATAAAAGATCTAGATGCAAGATTATTTTGGAT 843 604 AGGAGTGCACGGATAGCAAAACTAGAAAATGATACAAGAATTATTGAAGTTCTCTT 664 AAAGAATHAAHGIAAITITAGATGAGGEGAAAATGITTATITCAAAATITTATAGGT 904 AAAAGTAACCTTGATGAAGAGGTGAATGTAATTCCTCCACACACCACAGTTAGGACTG 1261 GTGAAGGATATAGGATACATCTTTAAAGAAAATTTG~TAAAAGTGTGTGGGACAGGGTTGT - Q ΩÇ ô a g qq 급 ð ζ ò δ g ò ò q ολ q ò qq g ò

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ACTACOCCECTAAATTETACTGCAAATGCAGACACACAACCTCAGCCTTCCAGACCCCACACACTCCAGACCCCACACACA	CHIAAA HOVAAA ICHIGAA YAO ATAAA OO ALTICHA HILIIHIIHIIHIIHIIHIIHIIHIIHIIHIIHIIHIIHI	ATTCCTGGAGGAACTCTATATTCACCCGGAACGCCATATAAAATTCAGAAGGT HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	CTCAAAAGAGGGGGGAAGGAAGGGGGGGGAAAAGGGAAAAAGGAGGGG
1684 1961 1744 1921 1804 1981 1864 2041 1924	2161 2161 2044 2221 2104 2281 2164 2341	2224 2401 2284 2461 2346 2521 2404	2581 2464 2641 2524 2701 2584 2764 2764 2764 2764
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hEST2; telomerase; catalytic subunit; reverse transcriptuse; life span; retinoblastoma; p53; tumour suppressor; inhibitor; arteriosclerosis; proliteration; immortal; tumour therapy; macular degeneration; activator;
2824 ATCTTGTGTAAATCCTGCCATTTAAAAAGTTGTAGCAGATTGTTTCTTCTTTTTGAAGTAA 2883
                                                                                        2884 AATTGCTGTGTTTATGGATAGTAAGAATGGCCCTAGAGTGGGAGTCCTGATAACCCAGG 2944
                                                                                                                3061 AATTGCTGTGTTTATGGATAGTAAGAATGGTCCTAGAGTCCTCATAACCACC 3120
                                                                                                                                                          3181 TAATTTATATGTATATTTTTAATTTAACATGAACACCCTTAGAAAATGTGTCCTATGT 3240
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                                                                                                         AAA29391 standard; DNA; 4839 BP.
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2000-400055/34

New method for increasing the proliferative capacity of cell lines comprises administering agents reversibly activating telemerase activity and reversibly inactivating ${\rm Rb/iNK4}$ and/or ${\rm p53}$ pathways useful in treating age related diseases

laim 5; Paqe 121-123; 123pp; English.

out, the number of mitotic divisions, of a cell, The method relies on activation of a telemerase activity and inhibition of one or both of a retinctional control of a set method satural pathway or a p53 pathway. Thospherylation of a by cyclin dependent kinases, cdk4 and cdk6, releases the cells into the division cycle. Binding of INK4 tamily members, e.g. the tumour sepressor pictures, inhibits kinase activity and results in growth arrest. We inactivators can setterively and reversibly inactivate an PEC NR1 pithway. Expecially as Edoplinkia pathway. The uncoprotein MOM2 is a cellular inhibitor of Mb/H2F function and the p51 tymour suppressor treat conditions related to (premature) ageing, e.g. macular degeneration lines in vitro and for studies on biochemical and physiological aspects or growth and differentiation. Long lived (immortal) cells could also be invention concerns methods and reagents for extending the lite-span. and can also be used in the methods. Other molecules which can be used include cdk4 or cdk6 mutants. In particular, a cdk4 mutant is one which differs from at one or more of residues K22, F34, H95 and 6 gar. increasing the proliferative capacity of cells. The cells are subsequently of use in pharmaceutical and cosmetic preparations used to Additional constructs include a papilloma virus E7 protein, or other virul oneoprotein which typasses Bb and/or pG3. Antisense constructs of and arterioselerosis. The cells can also be used to replace tumour cell The methods are useful for use in the production of normal or genetically engineered the Rb and pl61NK4a genes may also be used. biotechnology products.

Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other;

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3.2 OGGGAATOTGTATGTTTTATTGCAGGAGTTGAGGTGAGATGTGGTTGTTTTTTTGTTG 361 122 GGGAGGAGTTGGCTGTGGTGAGGGTTTGAAGAAAGAAGAAGAAGCTGATTTTACTG 181 182 CALLATGICAGAAAIIAAAGAIACCAGAICAIGTGAGAGAGAGAGAGCTIGGTTAACTTGGG 241 24.2 AGAAAGITTCATGTGGGATGGAGTATTGGGAGGTTATATTCAAAAGAAAAAGGAAAGTF 301 4.8. GONGAATOTOTATATOTTATTGOAGOAGTTGACCTAGATGAGAATGTGATTTTATTTACTG 492 452 AGCLAGAGAAAAAGATAGAAATGAGTGCATAAATTCTTTAAGCTTACTAAAAGAAATTG 421 422 ATACCAGTACCAAAGTTGATAATGCTATGTCAAGACTGTTGAAGAAGTATGATGTATTGT 481 4; Indels 177; Gaps Length 4839; Score 3182.6; DB 21, 0; Mismatches Pred No 0; 94.2%; Conservative Local Similarity Matches 3372; OHETY Match 3 9 3 Š ŝ Ş E 3 ي ŝ 4 35

1385 ATGTGCTTAATTTAAAAGCCTTTGATTTTTACAAAGTGATCGAAAGTTTTALCAAAGGAG 1444

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Oy Db	482 613	482 TTGCACTCTTCAGCAAATTGGAAAGACATGTGAACTTATATATTTGACACAACCCAGGA 541 	541
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do	733	TATTAGGTAAAGGGGAAGTATTAGAAATGGAAGAIGAIGTGGGTGATTTGATTTGAGTTAA	765
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Š	785	AACGATACGAAGAATTTATCTTAAAAATAAAGATCTAGATGCAAGATTATTTTGGATC	844
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ΟŊ	845	APIGATAAAACTCTTCAGACTGATTCTATAGACAGTTTTGAAACACAGAGAACACACAGAAA	904
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cy Db	905	AAASTAAPETTI GA USAABABISTAAATGTAATTOPTOPTOPAPATGTOAGTAASACTGTATA 	964
ó	965	TGAATA TA FORAATAATTAATGATTI IAAAITGAGGAAGIGAICAACCTTOAGAAA	1024
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Οy	1025	AICTGATTTCCTATTTTAACAACTGCACTGAATCAAAAGAAAG	1084
q	1333	ATCTGATTTCCTATTTTAACAACTGCACAGTGAATCCAAAAGAAAG	1392
90	1085	IGAAGGATATANAATAN'ATOTTTAAANGAGAATTTGOTAAGGOTGGGGGANAGGGTTGTG 	1144
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qq	1453	TOGABATTGGATCACGATACAAACTTGGATTCGCTTGTATTACCGAGTAATGGAAT	151
Oy	1205	CCATCCTTAATCAGAAGAAGAAGATTATCAATTCAAATTTTAGCAAACTTCTGAATG	1264
ď	1513	CONTGOTTAANTCAGAAGAAGAATTATCCATTCAAANTTTTAGCAAACTTCTGAATG	147
Q Q	1265	ACAACATTIICATAIGETCITIAIIGGGGGGGCCIGAGGTTGTAATGGGCCACATATA 	1324
ò d	1325	GCACAAGTACATCTCAGAATCTTGATTCTGGAACAGATITGTCTTTCCCALGGATTCTGA	1.484
ď	<u>.</u>	GCAGAAGTACATGTCAGAATCTTGALTCTGGAAGAATTTGTCTTTCCCATGGATTCTGA	169

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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             AAZ88444 standard; cDNA; 4839
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The present sequence encodes a human androgen receptor coactivator designated Rb. Androgen receptor to activator proteins from the present invention can be used in screening assays to identify candidate pharmaceutical molecules for the ability to promote or inhibit the interaction of androgen receptors and androgen responsive elements to modulate androgen receptors and androgen responsive elements to or activity. The identification and characterisation of androgen receptor co-activity autors such as those of the invention will treillitate the development of screening assays to evaluate the potential
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Novel androgen receptor-associated proteins used to detect androgenic
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Rb: androgenie: antiandrogenie, identification, prostate cancer; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     122 CGGAGGACCTGCCTCTCGTCAGGCTTGAGTTTGAAGAAACAGAAGAACCTGATTTAACTG 181
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     or untiandriaegic activity in screening assays for candidate pharmaccutical molecules which promote or inhibit the activity
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                                                                                                                                                                                                                                                                                                                                                                                    /note- "androgen receptor coactivator"
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                                                                                                                                                                                                                                                                                                                                   /product.- "Rb"
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                                                 Breast cancer related gene sequence SEQ ID No-1210
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The present invention describes a method (MI) for screening for an anti-neoplastic agent. The method involves exposing cells to a chemical agent to be fested for anti-neoplastic activity, determining a change in agents to be settled to a signature gene set, where (I) comprises a sequence (S) selected from 6447 sequences (given in Abribido) to the settlement of the fest of selected from 6447 sequences (given in Abribido) to the settlement of the settlement of the settlement of activity and can be used in quen inbrangy. MI can be used for screening a nati-neoplastic agent, and can be used for producing a product which is the data collected with respect to the anti-neoplastic agent as a crossit of MI, and the data is sufficient to couvey the chemical structure and/or properties of the agent. MI can be used in the structure and/or properties of the agent. MI can be used in the crossit such as colon, breast, stomach, lung, thyroid, oesophageal, ovarian, kidney, procale or panceatic cancer, adenorarian advances and many cell cancer, infiltrating ductal cancer, and militaring dobular cancer, squamous cell cancer, infiltrating ductal cancer.
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determining a change in expression of a gere of a signature gene set
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 F; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                               carcinoma, papillary carcinoma and Wilm's tumour.
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                                         Claim 1; SEQ ID 1210; 44pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Matric
Local Similarity 94.98;
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\$ - \$	785	AM GATA CAAGAAATTTATCTTAAAAATAAAGATCTAGATGCAAGATTATTTTGGATC 844 	
<u>خ</u> غ	845	ARGATAAAA TOTTOAGACTGATTOTATAGACAGTTTGAAACACAGAGAACACCAGGA 904 	
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× 4	127.8	TGANCACTATCCAACAATTAATGATGATGATTAAAATTCAGGAAGTGATCAACGTTCAGAAA 1024 	
् य	16.2%	AFCTGATTFCTATTTTAACAACTGCACAGTGAATGCAAAAGAAAGTATACTGAAAAGAG 1084 	
<u>بر</u> ءِ	1085	TGAAGGATATAGGATACATCTTTAAAGAGAAATTTGCTAAAGCTGTGGGAGAGGGTTGG 1144 	
ج غ	1145	TOGAAATEGRAFOACAGGRAFACAAACTFGGAGTTCGCTTGFATTACCGAGTAATGGAAT 1204 	
÷ ÷	1205	CCATGCTTAAATCAGAAGAAGAACATTATECATTCAAAATTTTAGCAAACTTCTGAATG 1264 	
<u> </u>	1265	ACAACATTITICATATOTCITIATIGGGGGGCCPTTGAGGTGGAAIGGGGACATATA 1324 	
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<u>خ</u> چَ	1485	ATGEGETTANTITAAAAGCCITTGATTTTACAAAGTGATGAAAGTTTTATCAAAGCAG 1444 	
5 8	1445	AAGGCAACHGAGAAAAAGAGAGAGAGAGAGAGGAGGAGAACAGGAACAGGGAAGGGAACAGGAACAGAGAGAGAGAGAGAGAAAAAA	
÷ 4	1505	AAFOCTTGCAFGGGTGTGAGATTGACTTTATTGATCTTATTAAACAATGAAAGGAGG 1564 	
<u>></u>	1565	GAGAAGACCAATGATGACTTGAATCTGCTTGTCTTAATCTTCCTCTCCAGAATA 1624	

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1933 ATCACACTGCACCACATALCTATCTTTCTCTGTAAGALTTCCAAAGAAAAAAAAATTTAA 1992
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1873 GAGAAGGAACCAACTGATCACCTTGAATCTGCTTGTCCTTTAATCTTCCTCTTCTTCTTGTAATA 1932
                                            1625 ATCACACTGAGCAGATALGTATGTTFCCGGTAAGALGAAGAAAAAAAAAAAAAAAA 1684
                                                                                                                           1685 CTACGCGTGTAAATTCTACTGCAAATGCAGAGACACAAAGGTCAGCTTCCAGACG 1744
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Meditied retinoblastoma tumeur suppressor, RISP protein, cancer therapy,
                    2705 TATGGCCACATTTAATATCTTCAGCTCTTTTTGTGGATATAAAATGTGCAGATGCAATTG 2764
                                                                           TITGGGTGATTGCTAAGGCACTTGAAATGTTAGTCATTGTTATTATACAAGATTGAAAA 2824
                                                                                                                                                    2825 ICHTGIGIAAAICCIGGGATTTAAAAAGTTGIAGGAGATTGTTTGCTCTTGCAAAGTAAA 2884
                                                                                                                                                                                             41.84 TCTTGTGTAAATCCTGCCATTTAAAAAGTTGTAGCAGATTGTTTCCTCTTCCAAAGTAAA 3192
                                                                                                                                                                                                                                 2885 ATTGGTGGGTTTATGGATAGTAAAAAAGGGGGTAAAAGTGGGAAGTGTGATAAACAGGG 2944
                                                                                                                                                                                                                                                                                                           2945 CTGTCTGACTACTTTGCCTTCTTGTAAAAAAAAAAGGCTCGCTGCTGGTTTTAAG 3004
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                 COSTITUTADA NA PROCANTITIGA TEGA COCCANTICA CO CANANTA TATACO TO ANA CONTRACTOR STORY
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              AAAATGGATATTATTAGAAATTAGAAAAATTACTAATTTTACACATTAGATTTTATT 3184
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                                                                                                                                                                    Modified retinoblastoma tumour suppressor gene.
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This sequence encodes a modified relimoblastoma tumour suppressor
protein (RTSP) of the invention. The proteins can be used for inhibiting
cellular proliferation, when coadministered with a p53 protein. The XTSPs
can be used for treating diseases characterised by abnormal cellular
proliferation, particularly cancers. The RTSPs have a broader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 121 COGGAGGACOTOCTOTOGGGGTTGAGTTTGAAGAAAGAAAGAAGAAGAGCTGATTTTACT 180
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      241 GAGAAAGTTTCATCTCCATGGAGTATTGGGAGGTTATTCAAAAGAAAAAAAGAACTG 300
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                361 GAGGTACAGAAAAACATAGAAATCAGTCCATAAATTCTTTAACTTACTAAAAGAATT 420
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    421 GATACCAGTACCAAAGTTCATAATGCTATGTGAAGACTGTTGAAGAAGTATGATGTATTG 480
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            481 TITTGCACTICITGAGGAAATTGGAAAGGACATGTGAACTTATATTTGACACAACCAGG 54U
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              481 TPFGCACTCTFCACCAAAFFGGAAAGGACATG1GAACTTATATATTFTGACACAACCAGC 540
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         361 GAGGTAGAGAAAAQATAGAATGAGTGTGCATAAATTGTTTAACTTACTAAAAGAAATT 420
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    6; Indels 177; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Ouery Match 94.2%; Score 3180.4; DB 19; Length 3554; Best Local Similarity 94.9%; Pred. No. 0; Matches 3371; Conservative 0; Mismatches 6; Indels 177; C
                                                                                                                                                                                                                     Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 3554 BP; 1170 A; 683 C; 653 G; 1048 I; 0 other;
                                                                                                                                                                                                                                        inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                         Claim 22; Page 226.230, 249pp; Unglish.
                                                                                                                             Ha S, Xu H, Zhou Y;
                                                                     (BAYU ) BAYLOR COLLEGE MEDICINE
                                                                                                                                                                                                                                                                                                                                                                                                        activity than wild type RTSPs.
                                    97US-003R118
 98WO-US03041
                                                                                          UNIV TEXAS SYSTEM
                                                                                                                                                               WP1; 1998-480788/41.
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                                                                                                                                                                                  P-PSDH; AAW69376.
                                                                                                                             Benedict WF,
19-FEB-1998;
                                    20-FER-1997;
                                                                                          (TEXA)
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Tue Jan 21 10:04:19 2003

548 720 603 780 780 780 723	783 960 1020 903 1080 963 1140 1200	1083 1260 1143 1320 1203 1380 1263 1323	1500 1383 1560 1443 1620 1503 1503 1563
	ITTATGAATICTCTTGGACTTGTAACATCTAATGGACTTCCAGAGGTTGAAAATCTTTCT TTTATGAATICTCTTGGACTTGTAACATCTAATGGACTTCCAGAGGTTGAAAAATCTTTCT AAACAACAACAAAAAATTATCTTAACAAAAAAAA		AND
549 541 721 721 604 781 664	724 901 784 961 904 1081 964	1024 1201 1084 1261 11144 1421 1204 1381	1441 1501 1501 1584 1561 1621 1504 1504
5 2 3 2 5 2 5 2		5 2 5 2 5 2 5 2 5	d 5 d 5 d 5 d 5 d

ćδ	1564	CGAGAAGGACCAACTGATCACCTTGAATCTGCTTTTTAATCTTCCTCTTCTAGAAT 1623	-
qu	1741	CGAGAAGGACCAACTGATTGATTGATTGATTGATTGATTG	2
ογ	1624	ANTCACACTICAGAGAGATATGTATGTTTCTTCTGTAAGATCTTCTAAAAAAAGGTTCA 1683	-
qq	1801	AATCACACTGCAGCAGATATGTATCTTTCTCTGTAAGALCTGCAAAGAAAAAAGGTTCA 1850	e e
ογ	1684	684 ACTACGCGTGTAAATTCTACTGCAATGCAGGAAAAAAAAA	~
qu	,1861	ACTACGGGGTGTAAATTGTACTGCAAATGCAGAGAAACAAGCAAG	0
ς	1744	CAGAAGCATTGAAATCTACTCTTTTACAGTGTTTATAAAAAAGGTALGGGCTAGC 1803	~
qq	1921	CAGAAGCCATTGAAATCTACCTCTCTTTCACTGTTTTATAAAAAGTGTATGGCTAGGC 1980	<u>_</u>
OY	1804	TATCTCCCCCTAAATACACTITGTCAACCCTICTCTCAACACCACAAATAAAAAT 1863	~
qq	1981	TATCTCCGGCTAAATACACTTTGTGAACGCGTTGTGTGAACACCAGAATTAGAACAT 2040	2
Οÿ	1864	ATCATCTGGACCCTTTTCCAGCACACACCTGCAGAATGAGTATGAATTCATTTTTTTT	~
пр	2043	APPLATORIGATION TO CARGAGACTO OF THE FINAL O	0
ογ	1924	CATTIGGACCAAATTAIGAIGIGTICCATGIATGGAAATGCAAAGIGAAGAAATAIAGAC 1983	-
q _Q	2101	CATTTGGACCAAATTATGATGTTCCATGTATGCCATATGCAAAGTGAAAGTATAGAA 2160	9
Ωŷ	1984	CTTAAATTCAAAATCATTGTAACAGCATAGAAGGATCTTCCTCATGCTGTTCTGGGGGAA 2043	-
qq	2161	CTIANATICAANATCATGIAACAGGATACAAGATCTTCCTCATGCTGTTCAGAGAGACA 2220	2
Οy	2044	TPCAAACGEGTTTTGATCAAAGAGGAGTATGATTGTATTATAGTATTCTATAACTTG 2103	-
qu	2221	TTCAAACGTGTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	2
λο 	2104	GTCTTCATGCAGAGACTGAAAACAAATATTTTGCAGTATGCTTCCACCAGGCCCCTACC 2163	~
ପୁର	2281	GTCTTCATGCAGAGACTGAAAACAAATATTTTGCAGTATGCTTTCACCAGGCCCGCGTACTTTTC 2340	0
δο.	2164	THEFT CACCANTACTICA CATAGORISM AND	~
qq ;	2341	TTGTCACCAATACCTCACATTCCTCGAAGCCCTTACAAGTTTCCTAGTTCACCCTTACGG 2400	9
oy	2224	AT POSTGORAGGRACATOTATATTTCAPCCCTGARGAGTCCATATAAAATTFTAGAAAGT 2283	Ξ
qu	2401	ATTICCTOGRACIOAACATCTATATTTICACCCTGAAGATCCATATAAAATTTICAGAAGGT 2460	2
δλ	2284	CIGCCAACACCAACAAAATGACICCAAGAICAAGAAICIIAGIIGIIGIIGIIGIIGIIGIIGIIGIIGIIGIIGIIG	~
qo	2461	CTGCCAACACAAAAATGACTCCAAGATCAAGATCTTAGTATCAATTGGTGAATCA 2520	2
OY	2344	THEGOGRACT TOTGAGAGIT COAGAAA LAAATOAGATGOTALGI AAGAAGAGAGGIG 2403	~
qq	2521	TTGGGGACITGTGAGAAJTGCAGAAAIAAAIGAAIGGTAIGIAACAG GAGGTGTG	9
ογ	2404	CTCAAAAQAAGTGCTGAAGGAAGCAACCTCCTAAAACAAAAAAATTAGTTTGTT 2463	
gci	2581	CTCAAAAGAAGTGCTGAAGGAAGGAAGCTCCTAAACACTGAAAAAAATTATTTTTTTT	Ξ
Qy	2464	ATTGAAGGATCAGATGAAGCAGAAGTAAACATCTCCCAGGAGAGTCCAAATTTCAG 2524	Ŧ.
qci	2641	ATTGAAGGALCAGALGAAGGAAGTAGAAGATGTGCCAAGGAGATGTAAATTTAA 2700	2
οy	2524	CACAAACTIGGGAGAAATGACTIGTACTIGGAAGGAAAAGAAAA	~
qq	2701	CAGAÂACTGGCAGAAATGACTTCTACTGGAACGGAATGCAAAAGCAGAAAATGAATG	ę
Οy	2584	AGGATGGATAGETCAAAGAAGAAGAGAAATGAGATGTAAGAAATTGGTGGACAGTG 2643	~
00	2761	AGCATGGATACCTICAAAGAAGAAGAAGAAGAGCATCTICAGGACTTTGGTGGACACTGT 2820	0
ò	2644	GTACACCTCTGGATTCATTGTCTCTCACAGAIGIGACIGIAIAACIIICO NGGITCTGT 2703	

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                                2704 HATGGPTAGATTFAATATCTTCAGCTCTTTTGTGGATATAAATGTGCAGATGCAATT 2763
                                                                                                                      2821 GIACACCTUTGGATTCATTGTCTCTCACAGATGTGACTGTATAACTTTGCCAGGTTGTGT 2880
                                                                    288] TIAIGGCCACAITIAATAICTICAGCICTIIITGIGGAIAIAAAAIGIGAAGII 2940
                                                                                                   2764 GITTGGGTGATTCCTAAGCCACTTGAAATGTTAGTCATTGTTATTATACAAGATTGAAA 2823
                                                                                                                                                                     2824 ATCITGTGTAAATCCTGCCATTTAAAAAGITGTAGCAGATGGTGCTGCTGCTGCAAAGIAA 2883
                                                                                                                                                                                                      0001 AICITGIGIAAATCCIGCCATITAAAAAGTIGIAGCAGAITGIITGCIGCAAAGIAA 3060
                                                                                                                                                                                                                                           2884 AA FEGOTETGOPPTATGGAFARAAAAAHGGOOOFAGAAGAAGGAAGFGAAAHGAFAAAGGG 2943
                                                                                                                                                                                                                                                          2944 CTGICTGACIACTIIGCCIICIIIIGIAGCAIAIAGGIGAICHIGGCIITGIIIIAI 3003
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    VERT TIACTATIGGAATCIGATATACIGIGGCTIGTTTIATAAATTTTGCTTTIAATTAAAT 3243
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    3244 AAAAGCIGGAAGCAAAGTATAACCATATGATACTATCATACTACTGAAAGAGATTTCATA 3303
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        3363 OCT CAGGAATGTAAAAGAACTTACTGATTATTTTCTTCATCCAACTTATGTTTTTAAATGA 3363
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Moditiod rotinoblastoma tumour suppressor: PTSD protoin:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Moditied retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  ellular proliferation inhibitor;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            AAVER451 standard; DNA; 3383 BP.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           **** SHAIIAIIGAIAGI 3377
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protein (RTSP) of the invention. The proteins can be used for inhibiting celliar proliferation, When condministered with a p59 protein. The RISis can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RTSPs have a broader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            421 GATACCAGTACCAAAGT1GAIAAIGC1AIGICAAGACIGIIGAAGAAGIAIGAIGIAIG 480
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         481 TITGCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATATTGACAACAAAGG 540
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            541 AGTITOCATGGTOGOTGGTTATATAGTTAATGGTTCAACTOGAAGAGOOGGAGGTGAG 6.0
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               541 AGITTGGATATGTAQTGAAATAAATTGCTGCATTGGTGGTTAAAAGTTTTGGTGAAAAGTTTTGTTGGAAAGTTTT 609
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         61 GAACCCCGGGTACTGCTGCCGCCCCCCTCCLGAGGACCCAGAGACACAGAGACAGACAGACAGCCCCG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       121 CCGGAGGACCTGCCTCTCGTCAGGCTTGAGTTTTGAAAACAGAAACCTGATTTTACT 180
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 241 GAGAAAGTITFATOTGIGGGAGIAIAITGGGAGAITATALICAAAAGAAAAAAAAAAAGIG 300
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   TGGGGAATCTGTATCTTTTGGAGGAGTTGAGGTAGAGATGTGGGTTGTCGTTTTTACT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   AND TGGGGAATCTGTATCTTTATGGCAGCAGTGACCTAGATGAGATGTCGTTCACTTTTACT
                                                                                                                                                                                                                                                                                                                            This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  93.8%; Score 3169; DB 19; Length 3383;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                Sequence 3383 RP; 1104 A; 657 C; 623 G; 999 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Mismatches 120;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Pred. No. 0;
                                                                                                                                                                                                                                                                                             Claim 22; Page 218 222, 249pp; English.
                                                                                                                                                        Ha S, Xu H, Zhou Y;
                                                                                                   (BAYU ) BAYLOR COLLEGE MEDICINE
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     0;
                                                                                                                                                                                                                                                                                                                                                                                                                 activity than wild type RTSPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 96.38;
                                  98WO-US03041
                                                                   97US-0038118
                                                                                                                    (TEXA ) UNIV TEXAS SYSTEM
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Matches 3257; Conservative
                                                                                                                                                                                       WP1; 1998-480788/41.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Local Similarity
                                                                                                                                                                                                         P-PSDB; AAW69375
                                                                                                                                                    Benedict WF,
                                19-FER-1998;
                                                                   20-FEB-1997;
27 - AUG - 1998
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601 AACAGGAGTGCACGAATAGCAAACAACTAGAAAATGAT-----ACAAGAAITATIGAA 654

099	714	774	834 840	900	954 960	1014 1020	1074 1080	1134	1194	ιά ν ρ	1314	1374 1380	ω 4	6 0	155 4 1560	1614 1620	167 4 1680	1734
TTAGETAAAGGGGAAGTATTAGAA	GTICTCTGTAAAGAACATGAATATAAGATGGGGGAAAAATGTTTGAAAAAT T 11 111	TITATAGOTITIATGAATTCTCTEGAGITGTAACATCTAATGGACTTCCAGAGGTIGAA 	AATCTITCTAAACGAIACGAAGAAATTTAICTIAAAAATAAAGATCIAGATGCAAGATTA 	TITTEGGA FRATGA IAAAACTETICAGACTGATTCI ATAGACAGTTTEGAAACAGAGA 	ACACCACGAAAAAGTAACCTTGATGAAGAGGGGAATGTAATTCCTCCACACACTGCAGTT 	AGGACTGITATGAACACTATCCAACAATTAATGATGATGATTAAAATTCAGAAGTGATCAA 	POTTE AGAAAA POGA HOOTA HII AACAACHGAACHGAATCCAAAAGAAAGTATA HII HII HII HII HII HII HII HII HII HII	CTGAAAAGAGTGAAGGATATAGGATACATCTTTAAAGAGAAATTTGCTAAAGCTGTGGGA 	PAGGETTGTGTGTGAAALIGGAPAYAGGALACAAACTTGGAGTTGGTGTGTATACGA 	GFAALGGAAITCALGCTFAAALCAGAAGAAGAAGGETFATCCATTCAAAATTTTAGCAAA 	CTECTGAATGACAACATTTTCATATGTCTTTATTGGGGGGGGG	GCLW-YITATAMCAGAAGTACAPCTCAGAATCTTGAATTCTGGAACAGATTGTGTTTGCCA 	IGGALPHGAARGGTTAAHTAAAAGCGTTGATTTTTACAAAGTGAFGTTTTTTTTTTTT	ATCAANGCAGAAGGCAA'TTGACAAGAAATGATAAAAACATTTAGAAGGATGTGAACAT - - - - - - - - - - - - - - - - - - -	GBAATCALGBAATCCCTTGCATGGCTCTCAGATTCACCTTTATTGATCTTATTAACAA 	PCAAADDACCAGAAGGACCAATIGATCACTIGAATCIGCTIGTGCTCTIAATCITICTTICTTICTTICTTICTTICTTICTTI	CTCCAGAATAATOACACTGCAGCAGATATGTATGTGTTGTCCGGGAAGATCTCCAAAGAAA 	AAAASTTCAACTACOGTGTAAATTCTACTGCAAATGCAGAGAGAAGAAGAACTCAGCC
Fo.1	5.5. 1.3.	715	775	7 + H	3.4.2 401	25.2 1.35.2	1015	1075	1145	1195 1201	1255	1415	1.675	1435	1495	1555	1615	1675
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1801 GGGTAGCCTAPCTGCGGGTAAATACACTTTGTGAAGGCCTTCTGTGTGTGAGGACTTAGAA 1860 2041 CAGGAGACATICAAACGIGITITGATCAAAGAAGAAGIAITAIGATITTAIAATATT 2100 2701 AGGITICIGITITATIGGCCACATITITAATATICITICAGCITITITITITITIGITGATATAAAATIGTGCA 2760 1855 TTAGAACATATCATCTGGACCTTTTCCAGCACACACACATGAGAATGAGTATGAACTCATG 1914 1975 AATATAGACCITAAATTCAAAAICATIGIAACAGCATACAAGGAICTTGCTCATGCTGTT 2044 2215 CCCTTACGGATTCCTGGAGGAACAICTATAITTCACTTCIGAAGAGTTCALATAAAATT 2274 2275 TCAGAAGGTPTGCCAACAACAAAAATGACTCCAAGATGAAGATFTTAGTATGAATT 2334 2455 CGCTTTGATATTGAAGGATGAGATGAAGTAGAAGTAAAGATGTCTCTAGGAGTGTC 2514 7697 1681 AAAGGTTCAACTACGCGTGTAAATTCTACTGCAAATGCAGGACACAAGCAACTCAGCC 1740 1735 TTCCAGACCCAGAAGCCATTGAAATCTACCTCTTTTTCACTGTTTAAAAAAGTGTAT 1794 1741 TTCCAGACCCAGAAGCCATTGAAATCTACCTCTTTCACTGTTTLATAAAAAAGTGTAT 1915 AGAGACAGGCATTTTGGACCAAATTATGATGTGTTCCATGTATGGCATATGGAAAGTGAAG 2095 TATAACTGGGTGTTCATGCAGAGACTGAAAGAAATATTTGGAGTALGCTTCCACCAG 2101 TATAACTGGGTGTTGATGGGGGGGGTGAAAAAAAAAATATTTGTATTTTAAGG 2155 CCCCCTACCTTGTCACCAALACCTCACATTCCTCGAAAGCCCTTACAAGTTTCCTAGTTCA 2281 TCAGAAGGTCTGCCAACACACAAAATGACTGCAAGATCAAGATCTTAGTATCAATT 2395 GACCGTGTGCTCAAAAGAAGTGCTGAAGGAAGCAAGCTGCTAAACTACTGAAAAAAATA 2575 ATGAATGATAGGATGGATAPGTCAAAQAAGGAAGAAATGAAGGATT CAGGAPPT PAGGAPPT PAG 2581 ATGAATGATASCATGGATACCTCAAAGAAGGAAGAAATGAGGATCTCAGGTTTTGGT 2635 GGACACTGTGTACACCTCTGGATTCATTCTCTCTCTCAGAGGGATGTGATAAATTTTCTC 2695 AGGTTCTGTTTATGGCCACATTTAATATCTTCAGCTCTTTTGTGGGATAIAAAATGTGAA ò q qq όy qq q 9 5 q ò <u>a</u> q: q ò 3 ć 9 ò q ò **a** <u>a</u> ò d ò ò Ôλ ò Ś qq ΟY ें ò ò

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2815. AGATTGAAAAFCTFGTGAAAFCCTGCCAFFTAAAAAGTTGTAGCAGTTGTTTGCTCTF 2874
                                                        POAAARIIAAAATTOPPOTOPPOTOTATOTATAAAAATGGOOTAGAAHOGGAHOOGA 2934
                                                                     1GT11T1A11AAFTTFAFAFGTAFFTFFFTFAAFTFFAACAFGAACACCCFFAGAAAAFGT 3054
                                                                                                                                                                                                     3000 IGTITITATIAATITATATATATITITITITAATITIAAARAAAATAT 3060
                                                                                                                                                                                                                                3055 CINCIAINIAICIICCAAATGCAATTTGATTGACTGCCCATTCACCAAAATTATCCTGAA 3114
                                                                                                                                                                                                                                                                                       3121 CTCTTCTGCAAAATGGAFATTATTAGAAATTAGAAAAAATTACTAATTTACAACATTA 3180
                                                                                                                                                                                                                                                                                                                                               1175 GALITITALI ITAGLAFFIGGAAFFFFGFFGFFGFFGFFGFFFFFFFTFATAAAAFFTFFGFFFF 3234
                                                                                                                                                                                                                                                                                                                                                                          (18) GAITITAITITACIATIGGAATOTGATATACIGIGGCTIGITITATAAAATITIGGITT 3240
                                                                                                                                                                                                                                                                                                                                                                                                       3235 JAATTAAATAAAAGCTGGAAGCAAAGTATAACCATATGATACTATGATACTGGAAACA 3294
                                                                                                                                                                                                                                                                                                                                                                                                                                                              4295 GATTTCATACCTCAGAAIGTAAAAGAACTTACTGATTATTTTCTTCAACCTAAGTTATGT 3354
                                                                                                                                                                                      Retinoblastoma; cancer; detection; diagnosis; protein, neoplasm,
                                                                                                                                                                                                                                                                                                                                                              (MASS ) MASSACHUSETTS EYE & EAR INFIRMARY.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       WHEL: ) WHITEHEAD INST BIOMEDICAL RES
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Location/Qualitiers
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Human retinoblastoma gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        assay: immune complex; ss
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A method for detecting the presence, in a tumour sample, of a protein
the absence of which is associated with a neoplasm, comprises
producing an antibody to the protein and then contacting the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           184 TTATGROAAATTAAAGATACCAGATCATGTCAGAGAGGGTTGGTTAGCTTGGGGA 243
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               244 AAAGTTTCATCTGTGGATGTATTGGGAGGTTATATTCAAAAGAAAAAGGAACTGTGG 303
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  304 GGAATCTGTATCTTTATGGAGGAGTTGACCTAGAGGAGATGTGGGTTCACTTTTACTGAG 363
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       5; Indels 180; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                 presence of the protein in the sample. The method may be used in the detection and treatment of a defective human gene related to
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                                                                                                                                                                                                                                             Immune complexes indicate the
                                                                      Diagnosing the presence of defective retincblashoma alleles -
                                                                                                                                                                                                                                                                                                                                                                          DB 15; Length 4597;
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                                                                                                         human retinoblastoma with DNA from a patient.
                                                                                                                                                                                                                                                                                                                                                                                                           0; Mismatches
                                                                                                                                                                                                                                                                                                                                                                      93.4%; Score 3153; 94.8%; Pred. No. 0;
                                                                                                                                               Example 2(2); Figure 7; 18pp; English.
                                                                                                                                                                                                                                                                                                   cancer, in particular retinoblastoma.
                                                                                                                                                                                                                                           antibody with the tumour sample.
                                                                                                                                                                                                                                                                                                                                                                                        Best Local Similarity 94.89
Matches 3366; Conservative
               WP*; 1994-272746,/34.
                                   P-PSDR; AARS8568
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2938 IGGGGALIGGTAAGGAATTGAAATGETAATTGTTATTTTATAGAAATGTTGAAAATG 2997
2245 TOGGEGATECCIAAGGCACTEGAAATGTTAGTCATTGTTATTATATAGACALGGAAAATG 2825
                                                           28. TIGIGIAAAICCIGOOAIIIAAAAAGIIGIAAAAIIGIIIGOIIIGCAAAAGIAAAAI 2886
                                                                           2947 GICTGACTACITTGCCTTCTTTGCATAGAGTGATGATGTTTGCTCTTGTTTTATAA 3006
                                                                                                                                                                                            4000 TITATATGIATATTTTTAATTTAACATGAACACCTTAGAAAAIGTGTGTATCTATC 3066
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                                                                                                                    288' 16CTG16C1FTATGGAFAGTAAGAAFTGGCGAGTCCFGATAACCGGGCF 2946
                                                                                                                                                                                                                                                                                                 3.2.3 TECCAAALGAAATIIGATIGACTGCCTAITCACCAAAATTATCCIGAACICTTCTCCTGCAAA 3126
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This is the nucleic acid sequence of a cDNA of the normal human retinoblastoma gene Rb. Absence or mutation of the Rb gene (see also ARAGACA) prodisposes an individual to retinoblastoma. To isolate Rb cDNA, the human DNA probe pH3-8, isolated from a human chromosome H3 lambda phage library, was used in a chromosome walk to isolate and map 30 kb of genomic DNA surrounding the H3-8 to isolate and map 30 kb of genomic DNA surrounding the H3-8 sequence. Fragment pDH30.7R (ATCC 97500) was obtained, and was used as a probe to sorrow a chNA therapy that had been constructed from an adenovirus 12-transformed human embryonic retinal cell from an adenovirus 12-transformed human embryonic retinal cell blots cross-reacted with a 4.7 kb transcript in transformed cells which was not present in 4 retinoblastoma and one corrows.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         deletion or point mutation in the Rb gene of a human patient. The gene can also be used to synthesize Rb polypeptide (see AAX01542) for
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          244 AAAGTTTCAPCTGTGGATGTATTGGGAGGTTAFATTCAAAAGAAAAAGGAACTGTGG 303
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     124 GAGGACCEGOCECTCAGGCTEGAGTEEGAAGAAAGAAGAACCEGATTTTACEGA 183
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             64 CHOCOGGRANDOROGOGOROPONTONTONGAGGAGGACCCAGGAGGACGACACCCCCCCCCC 123
                                                                                                                                                                                                                                                                              Isolated human retinoblastoma gene used to develop products for analysing predisposition to retinoblastoma and for the detection and treatment of retinoblastoma
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Indels 180; Caps
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           DB 20; Length 4597;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Match 93.4%; Score 3153; Di Local Similarity 94.8%; Pred, No. 0; es 3366; Consorvativo 0; Mismatches
                                                                                                                    (MASS-) MASSACHUSETTS EYE & EAR INFIRMARY.
                                                                                                                                                                             Dryja TP, Priend S, Yandell DW;
                                                                                                                                                                                                                                                                                                                                                               Claim 8; Fig 5; 32pp; English.
86US-0895163.
88US-0146525.
                                        89US-0300667.
                                                           92US-0951342
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                                                                                                                                         (WHED ) WHITEHEAD INST.
                                                                                                                                                                                                                   WPI; iqqq-nq4pqp,08.
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11-AUG-1986;
21 JAN 1988,
                                        23-JAN-1989;
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5 3	444		543	
5 3	144 25	100AT	548	
3	1.30		548	
<u> </u>	8. 1.	TTAGCTAAAGGGGAAGTATFACAAATGGAAGATGA	657	
	243		548	
<u>-</u> 2	853		717	
5 3	543 718	•	606	
0.7 0.8	7.07	AGTOCACOGALACCAAACAACTAGAAATGATAGAGAATTATTGAAGTTCTCTGTAAAATGATTTTTTTT	666	
5 2	6.6.7 8.18		726 897	
5 g	7.2.7 8.9.8		786 957	
5 3	787 958	GBTACGAAGAATTTAFCTTAAAAATAAAGATCTAGATGCAAGATTATTTTGGATCAT 	846 1017	
5 3	8477 10.18	GATAAAACTECTTAGACTGATTGTTAGAGAGTTTTGAAACACAGGAAAACAGAAAAAAAA	906	
5 3	1078		966 1137	
57	1967 1138		1026	
5 2	1027	CIGATTICCIATTITAA/AACTOCACAGIGAA IYCAAAAGAAAGTATACIGAAAAGAGIG TILLIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	1086	
50 G	1087	AAGGATATAGGATAGATGTTTAAAGGAGAAATTTGGTAAAGGTGTGGGGACAGGGTTGTGTT 		
5 ĝ	1147		1206	
5 G	1207		1266	
5 3	1267	AN'ATTITICATATGECTITATIGGCGTGGGCTCTTGAGGTTGTAATGGCGACATATAGC	1326	

1678 TCCCTIGCATGGCTCTCAGATTCACCTTATTTATTAAACAATCAAAGAACGA 1747 1387 GTGCTTAATTTAAAAGCCTTTGATTTTTACAAAGTGATGAAAGTTTTAT AAAGCAAA 1446 1507 TCCCTTGCATGCCTCTCAGALTCACCTTTALLTGALCTALLAAACAALCAAAGGACCA 1566 1567 GAAGGACCAACTGATCATCTTGATCTGCTTGTCTTAATCTTGCTTCTTCTTAATATAAT 1626 1627 CACACTGCAGCAGATATGTATCTTTCTCCTGTAAGATGTCCCAAAGAAAAAAGGTCAACT 1686 1798 CACACTGCAGCAGATATGTATCTTTCTCGTGTAAGAL TCCAAAGAAAAAAGTTCAACT 1857 1977 2398 CCTGGAGGAACATCTATATTCACCCCTGAAGAGTCCATATAAAATTTCAGAAGGTCTG 2457 1498 AGAAGTACATCTCAGAATCTTGATTCTGGAACAGATTTGTCTTTGCGATGGATTCTGAAT 1557 1858 ACGCGTGTAAATTCTACTGCAAAATGCAGAGAACACAAACCTCAGACCTTACAAACCAG 1917 1807 CICCGGCIAAAIACACIIIGIGAACGCCTICIGICIGAGCACCAGAAIIAGAACAIAI 1866 2158 AAATTCAAAATCATTGTAACAGCATACAAGGTCTTCCTGATGCTGTTCAGAAAATTC 2217 2287 CCAACACCAACAAAAATGACTCCAAGATCAAGAATGTTAGTATGAATTGGTGAAATCATTC 2346 2347 GGGACTTCTGAGAAGTTCCAGAAAATAAATCAGATGCTATGTAACAGGGGGGCGTGTGCTC 2406 2107 TTCATGCAGAGACTGAAAACAAATATTTTGCAGTAFFFFFCCACCACCACCTACTTG 2166 2227 CCTGGAGGGACATCTATATTTCAAGGGTGAAGAGTGCALATAAAAATTTCAGAAGGTCTG 2286 1327 AGAAGTACATCTCAGAATCTTGATTCTGGAACAGATTTGTCTTTGCCATGGALTCTGAAT 1380 1738 GANGACCAACYGAYCACCYGAAAGYGCTGCYCYTAACCYGACCAAAAAAA 1447 GGCAACTTGACAAGAGAAATGATAAAACATTTAGAACGATGTGAACATCGAATCATAGAA 1747 AAGCCATTGAAATCTACCTCTTTCACTGTTTTATAAAAAAGTGTATCGGCTAGCCTAT 2038 ATCTGGACCCTTTTCCAGGACACOCTGGAGAATGAGTATGAACTCATGAGAGACACAT 1927 TTGGACCAAATTATGATGTGTTCCATGTATGCCATATGCAAAGTGAAGAATATAGACGTT 2098 TEGGACCAAATEATGALGICITEGATGTALGGGALATGATGAAAGTGAAAATATAGAATTA 2047 AAACGTGTTTTGATCAAAGAAGAGGTATGTATTGTATTATTAGTTATTAACTCGGTC 2167 TCACCAATACCECACATICCICGAAGCCTIACAAGTITCCIAGITCACCCITACAATI q ć Q 2 ò qq ò qq ó 9 qq ò q ć qq δ qq qq q $^{\circ}_{\lambda}$ d q qq ò qq ŝ δ ò Ś q ò ò q ò ò Οy

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1578 AAAAGAANTGTTGAAGGAAGNANOCYOOTAAANGAYTGAAAAAANTAGGGYYTYGATATT 2637
                                                     2467 GAAGGALPAGATGAAGPAGATGGAAAGTAAACATGTGGGAGGGAGAGTGGGAAATTTGAGGAG 2526
                                                                                        2638 GAAGGATCAGATGAAGCAGATGGAAGTAATATTTTTTAGAAGAGAGAATTTOAGAAG
                                                                                                                         2587 ATGGATACTTCAAACAAAGAAAAAAAAAAAAAAAAGAATCTCAAGACTTGGEGGGACACTGTGTA 2646
                                                                                                                                                                                                              2758 ATGGATACTCAAAAAAASAASAA BSAGGATCTCAGGOOTTGGT SACAGTA 2817
                                                                                                                                                                                                                                                                  2647 CACCTCTGGATTCATTGTCTCTCACAGATGTGACTGTATAACTTTCCCCAGGTTCTGTTTA 2706
                                                                                                                                                                                                                                                                                     2787 TGGCCACATTTAATATCTTCAACTCTTGAATATATAAAATGTGCAGAATGTTTT 2756
                                                                                                                                                                                                                                                                                                                                                         2767 IGRGIGATITETIAAGEEAFFIFFAAAFFIFFAGIGATTATTATATATATAAAAATC 2826
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                                                                                                                                                                                                                                                                                                                                                                                                                                            2938 IGGGTGATTCCTAAGCCACTTGAAATGTTAGTCATTGTTATTATACAAGATTGAAAATC 2997
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     2886
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        2947 GICIGACTACTITGCCTICTITGIAGAGATATAGGAGATGTFGGTGTTTGTTTTTATTAA 3006
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  4298 AATGGATALTATTAGAAATTAGAAAAATTACTAATTTTACACATTAGATTTTATTA 3357
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     3247 ABCTGGAABCAAAGTATAACCATATGATACTATCATACTACTGAAACAGATTTCATACCT 3306
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Diagnosis of retinoblastoma · using genetic material corresp. to a normal
human retinoblastoma gene or a unique sub-region
                                                                                                                                                                                                                                                                                                                                                                                                                                                       This gene encodes a protein, the absence of which is associated with a neoplasm. It is used to produce an autibod, to the protein, contacting this with the tumour sample and detecting immune complexes as indication of the presence in the tumour sample of the protein. Whole sequence or a unique sub-region can be used. The method identifies patients lacking the defective retinoblastoma (Rb) allele and thus are not at risk of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             177
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       244 AAAGTITCATCHGGGATGGAGTAFFGGGAGGFFFATTCAAAAGGAAAAGGAACTGTGG 303
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Indels 180; Gaps
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 4597 BP; 1489 A; 839 C; 815 G; 1454 T; 0 other;
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                                                                Retinoblastoma; neoplasm, osteocarcoma; ss.
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                                                                                                                     Lucation/Qualifiers
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3	6.6.7	GAACATGAATGTAATATAGATGAGGTGAAAAATGTTTATTTCAAAAATTTTATACCTTTT	726
â	x x	GAA'ATGAATGTAATATAGATGAGAGGAAAATGTTATTCAAAAATTTATAGCCTTT	897
3 3	127	ATGAATTCTCTTGGACTTGTAACATCTAATGGACTTCCAGAGGTGAAAATCTTTCTAAA 	786
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ŝ	1018	GATAAAACTCI FCAGACTGATTCI ATAGACAGII FTGAAACACAGAGACAGAGAGAAAAA	1077
5 2	1078	AGTAACCTEGATGAAGADGAATGTAATTCCTCCACACACTCCAGTTAGGACTGTATG	966 11 47
53	146	AAMANTEATOTAANAATTAATIGATTTTAAATTOAGGAAGTGATGAAGCGTFCAGAAAAT	1026
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5	1027	CTGATTTCCTATTTAACAACTGCACAGTGAACAAAAGAAAAGTATACTGAAAAGGGGG	1086
ş	1198	CHALLICOLATITIAACAACIGCACAGIGAATICCAAAAGAAAATATAGIGAAAAAGAGTG	1257
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5 2	1207	ATG/TTAAATCAGAAGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGAC 	1266
έş	1267	ANYATTITICATAIGECITTATIGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG	1326

ପୁପ	1438	AACATTITICATATGTCTTATTGGCGTGCGCTCTTGAGGTTGTAATGGCCACATATAGC	1497
δλ	1327	AGAACIACATCTCAGAATCTTGATTCTTGGAACAGATTTGTCTTTTCTCATGGATTCTGAAT	1 386
qc	1498	AGAAGTACATCTCAGAATCTTCATTCTGGAACAGATTTGTCTTTCCCATGGATTCTGGATT	15,47
ογ	1387	GTGCTTAATITAAAAGCCTTGATTTTACAAAGTGATCGAAAGTTTTATCAAAGAAAAAAAA	1446
qg	1558	GTGCTTAATTTTAAAAGCCTTTGATTTTTACAAAGTGATCGAAGAGTTTTATCAAACAGAA	1617
Оγ	1447	GGCAACTTGACAAGAGAAA GATAAAAACA LTTAGAAGGAT GTGAACA LGGAA TATAGAA	1506
Ob	1618	GGCAACTTGACAAGAGAATGATAAAACATTTAGAACGATGTGAACATCGAATGAGAA	16.77
ОУ	1507	TCCCTTCCATGGCTCTCAGATTCAGCTTTATTCATCTAAACAATGAAAGGACGA	1566
of G	1678	TOCCTT GCATGGCTCTCAGT TCACCTTTATT TGALCTT AATAATAA CAAAAGAAAAGA	17 47
ò	1567	GAAGGACCAACTGATCACCTTGAATCTGCTTGTTAATCTTCTTCTCTCTC	1626
qq	1738	GAAGGACCAACTGATCAGCTTGATCTGCTGTGATGTTGTTCTTCTGTGGAATAAT	1797
δλ	1627	CACACT GCAGCAGA LA LG LATCTT CTCCTGTAAGATCTTCCAAGAAAAAAGTT CAACT	1686
Q Q	1798	CACACTGOAGCAGATATGTTTGTTGTTGTAAGATGTGGAAAGAAAAAGGTTGAGT	1857
Óγ	1687	ACCCTICTARATITICTACTIONAATICACACACACAACCTICACATITICATARACACA	1746
qo	1858	ACGCGTGTFAATTCTACTGCAAATGCAGAGACAAAGCAAGCTCAAGCTTCCAGACGAG	1417
λο	1747	AAGCCATTGAAATCTACCTCTCTTTCACTGTTTATAAAAAAGTGTATCGGCTAGCCTAT	1806
qc -	1918	AAGCCATTGAAAHCTACCTCTTTTCACTGTTTTALAAAAAGTGTALGGGCTAGCTAT	1477
ó,	1807	CPCCGGCPAAATACACTTTGTGAACGCCTTCTGAGCTGAG	1866
ୁଧ୍ୟ <u>.</u>	1978	CTCCGGCTAAATACACTTTGTGAACGCCTTCTGTCTGAGCACCGCAAATTAGAACATAT	2037
оу	1867	ATCTGGACCCTTTTCCAGGACACACCGTGCAGAATGAGTTGATGAACTCATGAGAGAGA	1926
qa	2038	ATC1GGACCCTTTTCCAGCACACCCTGCAGAATGAGTATGAACTCATGAGGACACT	2097
δ	1927	TTGGACCAAATATGAGGTGTTCCATGTATGGCATATGCAAAGTGAAGAATATAGACTT	1986
<u>a</u>	2098	TTGGACCAAATTATGATGTGTGTGTATGCAAATGCAAAGTGAAGAATATAGACTT	2157
Οy	1987	AAATTCAAAATCATTGTAACAGGTACAAGGTCTTCTTCTTCTTGTGTGTG	2046
qc	2158	AAATTCAAAATCATTGTAACAGCATACAAGGA FCTTCCTCATGCTGTTCAGGGACACATTC	2217
Oy	2047	AAACGTGTTTTCATCAAACAAGAGGAGTATGATTCTATTATAGTATTCTATAACTTCGGG	2106
a	221B	AAACGIGII FIGAFCAAAGAAGAGAGIAIGA HITTA HAHALIA HATAAA HAGIGI	1.577
ò	2107	TTCATGCAGAGACTGAAAACAAATTTTGCAGTATGCTTCCACCAGGCCCCCTACCTG	2166
q	2278	TTCATGCAGAGACTGAAAAAAAAAAAAAAAAAAAAAAAA	2117
Оу	2167	TCACCAATACTICACATTCCTCGAAGCCCTTACAAGTTTCTTACTTTTTTTT	2226
qq	2338	TCACCATACCTCACATICCTCGAAGCCCTTACAAGTTGCTAGTTCACCTTACAGTT	64.7
ΟŸ	2227	CCTCGACGAACATCTATATTTCACCCTGAAGAGTCCATATAAAATTTCAGAAAACTG	9822
qn	2398	CCTGGAGGAACALCTATATTCACCCTGAAGACTCTATATATATTTCACAAGTTTC	2457
ογ	2287	CCAACACCAACAAAAAAGGCCAAGAICAAGAAATCTIAGIAICAATGGAATCATTC	2346
qq	2458	CCAACAACAAAAAIGACII CCAAGAII CAAGAAI CII I AGI ATGAAI I GGI GAATI CATI	2517
QY	2347	CGGACITICTGAGAAATICAGATCAGATGGTATGTAAATGAAAGAAAGAAAGAAAGAA	2406
qq	2518	GGGACTTCTGAGAAGTTCCAGAAAATAAATCAGATGGTATGTAACAGACGACGTGTGTC	25,77

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2879 AAAAQAAQ GOTGAAQQAAQQAAQQAAQQAQTGAAAAQQAQTGAAAAAQCTGTGAAATT 2637
24.7 AAAAGAAGTGCTGAAGGAAGCCTCCTAAAACCACTGAAAAAACTACGCTTTGATATT 2466
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ABERRANTS Standard: CDNA: 4740 BP.

RESULT 12 ABKB6079 ID ABK80

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The invention relates to an anticancer agent comprising mycolactone. Also included for is an arriagner agent comprising mycolactone and antisanse inhibitors of relinchlastoma (Rb) protein expression. The anticancer agent is used for the treatment of cancers such as breast, bladder, skin, stommen, liver, colon and oral cavity, lymphoma and cukaemia. The anticancer agent induces apoptotic death of cancer cells and the Rb inhibitor increases the apoptotic death of cancer mycolarone are in the Rb inhibitor ancer apoptotic fact in grand is specific to cancers in which Rb proteins are optionally expressed and mycolactone shows very strong anticancer effect in gite as well as in gro.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         254 CGGAGGACCTGCCTCTCGTCAGGCTTGAGTTTGAAGAACAGAAGCTGATTTTTACTG 313
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              374 AGAAACHTHEATETGTGTATHGGGAGGTTATTCAAAAGAAAAGGAAAAGGAACIGT 433
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  122 GGGAGGACTGCTCTCGTCAGGIIGAGIIIGAAGAAAGAGAAGCIGATIIIACIG 181
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    ND GRIGAATCTGTATCTTTATCGCAGCAGTTGACCTAGATGAGATGTCGTCGTTCACTTTACTG 361
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               11; Indels 179; Gaps
                                                                                                                Human, relinchlastema protein, RE, citostatic, camer, apoptosis, mycolactone, antisense; breast cancer, bladder cancer, skin cancer, stomach cancer, liver cancer, colon cancer; cral cavity cuscer;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      The present sequence is the human cDNA for retinoblastoms protein.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            242 AGAAAGTTTGATGTGGAVGGAGTATTGGGAGGTTATATTGAAAAGAAAAGGAACTGT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     93.2%; Score 3148.4; DB 24; Length 4740; 94.7%; Pred. No. 0;
tive 0; Mismatches 11; Indels 179; C
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Anticancer agent useful for treatment of cancer e.g. of skin,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Sequence 4740 BP, 1508 A, 887 C, 862 G, 1453 i, 0 other;
                                                                                 Human retinoblastoma protein cDNA sequence.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Example 4; Page 38-42; 44pp; English.
                                                                                                                                                                        lymphoma; leukaemia; gene; ss.
                                                                                                                                                                                                                                                                                                              23-NOV-2001; 2001WG KR02026.
                                                                                                                                                                                                                                                                                                                                                  23-NOV-2000; 2000KR-0070089.
                                                                                                                                                                                                                                                                                                                                                                    2000KR-0080184.
                                                 (first entry)
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                                                                                                                                                                                                                                                                                                                                                                                                     (BIOG-) BIOGENIA CO LTD
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               comprising mycolactone
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Local Similarity
                                                                                                                                                                                                                                          WO200241888-A1.
                                                                                                                                                                                                         Homo sapiens.
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Ē	1214	AAAAGTAACTGAAGAAAAGGGAATAGATGCGCGCGCACACAGTAGGATTAGGTT 1272	
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đ	1513	VTGCTTAAATCAGAAGAAGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAAT
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qq ,	157 3	
ς	1324	AGCAGAAATACATCAGAATCTTGALICTGGAACAAATTTGTCTTTG CALGAATTCTG 1883
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. δ •••	1384	AATGTGCTTAATTTAAAAGCCTTTGATTTTTACAAACTGATCGAAAGTTTTATAAAGCA 1443
අ :	1693	AATGEGETAATTTAAAAGGCTTGATTTTTAGAAAGGGTGGAAAGTTTATGAAGGC 1752
οy	1444	GAAGGCAACTIGACAAGAGAAAAAGATATAAAAAATTAAAAAGATGTGAAAAAA
qc	1753	GAAGGCAACI IGACAAGAGAAAIGATAAAAGATTTAGAAGGATGTGAACATCGAATCATG 1812
Ογ	1504	GAATCCCTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAACAACAATGAAGAC 1563
q	1813	GANTCCCTTGCATGCCTCTCAGATTCACTTTALTTGATCTTALTAAAAAATAAAAAAAAAA
ΟŸ	1564	rgagaaggaggaagagargaggiigaajgidki jalkiti jalaajki jirkiki jirikaaaa 1623
Db	1874	CGAGAAGGCCAACTGATCACCTTGAATCTGCTTGTGCTTTAATCTTCCTCTCAGATTT932
οy	1624	AATCACACTGCAGCAGATATGTATCTTTCTCCTATAAGATCTCCAAAGAAAAAAGGTTCA 1683
10b	1933	AHTERTETETETETETETETETETETETETETETETETETE
00	1684	ACTAGGGTGTAATTCTAGTGGAATGCAGAAATAAGTAACCTGAGCTTAACTTATATATA
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ςy	1744	CAGAAGCATIGAAATGIACTCTCTTTCACTGIIITATAAAAAGTGTATAAAAAAGTGTATAACT 1803
qq	2053	CASARAGCATTGAATCTACTCTTTCACTCTTTATAAAAAAGGTATATATA
οy	1804	TATCHCGGCTAAATACACTTTGTGAACGCCTTCTGTCTGAACACACAAATTAGAAATTAGAATTTAGAATTTAGAATTTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTTAGAATTAGAATTTAGAAT
qu	2113	TATCTCCGCCTAATTACACTTTCTTCTCTCTCTCTCTCTC
ò	1864	ATCATCHGGACCTITICCAGCACACCCTGCAGAATGAGTATGAACTCATGAGACAGG 1923
qo	2173	ATCATCTGGACCCTTT FCCAGGACACACGGGAAATGAGTATGAAGTCATGAAGAGACACACA
ΟŸ	1924	CATITIOGACCAAATTATGATGTGTTCCATGTALGGAAATTGCAAAGTGAAGAATATAGGC 1983
ପ୍ପ	2233	CATTECCACAAATTATGATGTGTTCCATGTATGCAAAAGTGAAGAAATATAGAG 2292
QY	1984	CUTAAATTCAAAATCATGTAACAGCATACAAGCATOTTOTTGATGATGTTOTTOTTOTTOTTOTTOTTOTTOTTOTTOTTOTTOTT
qn	2293	CLIMANTICAMANICALIGIAACAOCALACAAGALCHIGCHCHIGCHCANGAGAAA 2352
Ś	2044	TTCAAACGTGTTTGATCAAAGAAGGAGTAGATTCTATTATAGTATTCTAGTAGTCG 2103
qu	2353	TECAAACGEGETTEGATCAAAGAAGAGGAGTATGATTATAGTATTCTATAAGTCG 2412
ΟY	2104	OPCHECALGCAGAGACEGAAAACAAATHTTTCCAGTACCTTCCACTAGGGGCCCCTTACCTTA
qq	2413	GECTTCATGCAGGAGTGAAAAAAAATATTTTGCAGTATTCCACCAGGCCCCGTACC 2472
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qu	2533	ATTICCTIGGAGGGAACATCTATATTTCACCCCTGAGACTCCATATAAAALTTCAGAAGGT 2592
ΟY	2284	CTGCCAACACCAACAAAATGACTCCAACATCATAAATCTTAGTATCAATTGCTGAATCA 2343
qo	2593	CTGCCAACACCAACAAAATGACTCCAAGATCAAGAATCTTAGTATCAATTGCTAATCA 2652

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2453 PPPOPARA POTCAGARAN POT ANA ANA ANA BARANSHANSHANSHANSHANGAGAGG POT 2712
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2713 CTCAAAAGAAGTGCTGAAGGAAGAAGCTGTGTTAAACGACTGGAAAAAAACGTGGGTTTGAT 2772
                                                                                                                                                                                                 214.1 APTICAAGTATCAAGGAGAGTAAGTAAAGTAAAGATCTTTTTTTAGGAGTTTTGAG 2523
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protein (RISP) of the invention. The proteins can be used for inhibiting callular proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
                                                                                                                         Modified retinoblastoma tymour suppresser, PTSP protein, concertiberapy,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  241 GAGAAAGTTTCAICTGTGGATGGAGTAITGGGAGGTAAITCAAAAGAAAAAAAAAGAACIG 300
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      This sequence encodes a modified retinublastuma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                        Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 92.1%; Score 3111; DB 19; Length 3347; 95.9%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 3347 BP: 1096 A: 650 c; 617 d; 984 T; 0 other;
                                                                                                Modified retinoblastoma tomour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Claim LL; Fage 196-200, 249pp, English.
                                                                                                                                       cellular proliferation inhibitor; ss.
                                                                                                                                                                                       Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                             Benedict WF, Hu S, Xu H, Zhou Y;
                       AAVS8448 standard, DNA; 3347 BP.
                                                                                                                                                                                                                                                                                                                                         (BAYU ) BAYLOR COLLEGE MEDICINE.
                                                                                                                                                                                                                                                                                         98W0-US03041
                                                                                                                                                                                                                                                                                                                97US-0038118
                                                                        UL-DEC-1998 (first entry)
                                                                                                                                                                                                                 đ
                                                                                                                                                                                                                                                                                                                                                    (TEXA ) UNIV TEXAS SYSTEM
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Matches 3237; Conservative
                                                                                                                                                                                                 ..2586
                                                                                                                                                                                                             /*t.ag-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Local Similarity
                                                                                                                                                                                                                                                                                                                                                                                                     WPI; 1998-480788/41.
                                                                                                                                                                                                                                                                                                                                                                                                                  P-PSDB; AAW69372.
                                                                                                                                                                Homo sapiens
                                                                                                                                                                                                                                                                                         19-FEB-199R;
                                                                                                                                                                                                                                                                                                                20-FEB-1997;
                                                                                                                                                                                                                                      WO9837091-A2
                                                                                                                                                                                                                                                                 27-AUG-1998.
                                                AAV58448;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Query Match
RESULT 13
          AAV58448
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27, 16.1	NJCTACAGAAAACATAGAAATCAGTGCCATAAATTCTTTAACTTACTAAAAAAA	420
46.1		; x
417		· •
4B1	TATA' AAAG	540 521
541	ACTICGATGGTCGCTGTTATACCATTAATGGTCACCTCGAACAACCCAGGCGAGGTCAG	600 570
501	AAPAGGAGTOCAGGGATAGFAAAAGAAGTAGAAATGATAGAAGAATTATTOGAGTTOC TELEHTELLITTITTITTITTITTITTITTITTITTITTITTITTIT	660 630
149	TGTAAAGAACATGAATGTAATATAGATGAGGGGGAAAAATGTTTATTTCAAAAATTTTATATA	720
7.21	CCTITIAGGAATICTCTGGACTIGTAAGACTGGAGGGGTGCGAGAGGTGAAAALCTT 	780
75.1	CCTAAACGALAGGAAGAAATTTALGTTAAAAATAAAGALCTAGATGGAAGATTATTTTG FFFFFFFFFFFFFFFFFFFF	840
я 1 н	GAFCATGATAAAACTGTTGAGACTGATTGTATAGAGAGTTTTGAAACACAGAGAAGAACACA FELFELFELFELFELFELFELFELFELFELFELFELFELF	900
901	GGAAAAAGTAAGCTGAAGAAGGGAATGTAATICCTGGAGAGACTCGGGTTAGGACT 	930
961	GTTALGACCACTALCCACCATTCATGALTTTAAATTCAGCAAGTGATCACCTTGATTTTAATTCAGCAAGTGATCAACCTTGATTTAAATTCAGCAAGTAATTCAATTCAACTTTAAATTCAGCAAGATTAAAGATGATTTAAATTCAGCAAGTAACTTCA	1020 990
1621	GAAAATCTGATTTCCTATTTTAACAACTGGACAGTGAATCGAAAAGAAAG	1080
1081	AGASTGAAGGATATAGGATACATCTTTAAAGAAATTTGCTAAAGCTGTGGGACAGGGT - - - - - - - - - - - - - - - - - - -	1140
1141	TOTAL CAAATTO SALCAVOCATACAAACTIGGAGI COCTTGTATTACCGAGTAATG TITTITITITITITITITITITITITITITITITITI	1200
1201	GAATCCATGCTTAAATCAGAAGAAGAAGGATTATGCATTCAAAATTTTAGGAAACTTCTG FFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	1260
1261	AATGACAACAIITITCAIATAGATTITIATGACGIGGGCICTTGAGGTGTAGAGGCCACA	1320
1321	FATADEAGAACHACAGAALCEIGAHCIGGAACATHGICHTEGCAIGGATT 	1380 1350

ά	1381	381 CTGAATGTGCTTAATTTAAAAGCTTTGATTTTTAVAAAGTGATCGAAAGTTTTALCAAA 1440	1440
<u>a</u>	1351	CTGAATGTGCTTAATTTAAAAGCTTTGATTTTTACAAAGTGATCGAAAGTTTTATCAAA 14	2
ΟŸ	1441	GCAGAAGGAACTTGACAAGAGAATGATAAAATATTTAGAAGGAGGAAGATGATGAT	500
QQ Q	1411	GCAGAAGGCAACTTGACAAGAAATGATAAAACATTTAGAACGATGTGAACATGTGAATG 14	470
ΟŅ	1501	ATGGATCCCTTGCATGGCTCTCAGATCACCTTATTGATCTTATTAAACAAG 15	260
વલ	1471	AIGGAAICCCTIGCAIGGCTCTCAGALLCACCTLIALLIGAICTTALLAAGAATTAAA	Ç Ç
ογ	1561	GACCGAGAAGGACCAACTGATGAATCTGTTGTCTTTAATCTTATATCTTCTTAATCTTGTTTA	620
qu	1531	GACCGAGAACGACCACTTTTTTTTTTTTTTTTTTTTTTT	0.65
Оу	1621	AATAATGACACTGCAGCAGATATGTATCTTTCTCTGTAAAATGTCTCCAAAAAAAA	989
qq	1591	AATAATCACACACACACACATTTTTTTCTCCTGIAAGATCTCCCAAAAAAAAAA	0.50
ογ	1681	TCAACTACGCGTGTAAATICTACTGCAAATGCAGAGAAAAGGAACCTCAGCTTCAG 17	740
qq	1651	TCAACTAGGGGGGAAATTGTAGGAAATGGAGAGAAGAAGAAGTGGGTTTGGGTTT	710
δλ	1741	ACCCAGARGCCATIGAAATCTACCTCTTTCACTGTTTATAAAAAGGTGTAFGGGTA 18	406
00 10	1711	ACCAGAAGCATTGAAATGTACCTCTTTCACTGTTTTAAAAAAGTGTATGGATA 17	077
ОУ	1801	GCCTATCFCCGGCLAAATACACTTTGTGAACGCTTTCLGTCTGAGCACCAGAATTAGAAA TB	96.0
QQ	1771	GOCTATCTCCGGGTAAATACACTTTGTGAACGCCTTCTGTGTTGGGACCCAAGAATTAGAA 18	3.40
ΟŸ	1861	CATATCATCATCATCATCATTTTCCAGCACACCTCAGAATGACTATGAACTCATGAGACTT	076
qu	1831	CATATCATCHGGACCTTTTCCAGCACACTCTAAAATGACTATGAATTAAAAAAA 18	340
δ	1921	AGGCATTTGGACCAAATTATGATGTGTTCCATGTATGGCATATGCAAAGTGAAGAATATA 19	OH
00	1891	AGGCATTTGGACCAAATTATGATGTTGTTGTATGTATGTA	950
ОУ	1981	GACCTTAAATTCAAAATCATTGTAACAAAAAAGATCTTGGTATGTGTGTG	040
qq	1951	GACCTIAAATICAAAATCATGTAACAGCATACAAGGATCITCCTCATGCTGTTCAGGAG 20	010
ογ	2041	ACATTCAAACGTGTTTTGATCAAAGAAGAGGAGTATGATTCATTATAGTATTATAAC 21	100
QQ	2011	ACATTCAAACGIGTTTTGAICAAAGAAGAGGAGTATGATTCTALIALAGIATTCTALAAAC 20	070
δγ	2101	TORGICITCATGARGAGA GAAAAAAAAATATIITGAGATATGCITCAGCAGGCCCCT 21	160
qq	2071	TEGGICITICATGCAGAGAGTGAAAAGAAATATTTTGCAGTATGCTTPPAPGAGAPGCT_21	130
Οy	2161	ACCITICTORCAATACCICAAATTCCTCAAACCCIIAAAACTTICTAACTTICTAAAATAA 22	520
qq	2131	ACCTTGTCACCAATACCTCAAATTCCTCGAAGCCCTTACAAGTTTCCTAGTTCACCTTA 21	06.1
ολ	c:	COSATTOPI SCAGGOAACA PITATAT TIPOACHORIOAAGAD COATATAAAAT FINAGAA 22	087
qu	2191	CGGATTCCTGGAGGAACATCTATTTTCACCCTGAAGAGTCCATATAAAATTTCAGAA 22	057
ο̈́	2281	GGTCTGGCAACAACAAAAAIGACTGGAAGATGAAGAATGTTAGTATGATGATGAAAAAAAA	0.41
qq	2251	GGTCTGCCAACAACAAAAATGACTCGAAGATCAAGAATCTTAGTATCAATTGTTTTTTTT	013
οy	2341	TCATTCGGGACTTCTGAGAAGTTCCAGAAAJAAATGATGGTATGTAAAAAAAAAA	40.0
qq	2311	TCATTCGGGACTCTGAGAAGTTCCAGAAAAAAATCAGATGGTATGTAACAGGGACGT 23	17.0
ΟŅ	2401	GFGCTCAAAGAAGTGCTGAAGGAAGCAACCT\\\\\\\\\\\	160
qu	2371	GTGCTCAAAAGAAGTGCTGAAAGGAAACCTGCTAAAGTACTGAAAAAAATAAGTTT 24	3.0
ζò	2461	GATATTGAAGGATCAGATGAAGCAGATGGAAGTAAACATCTCCCAGGAGAGTCAAAATTT 25	220

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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   2641 IGIGIACACTCIGGATTCATTCTCTCACACATGNGACTGTATAACTTCCCCAGGTTC 2700
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       27-0 TGTTTATGGCCACALITAAIAICIICAGCICIIITIGIGGAAIAIAAAAIG1GCAGAIGCA 2760
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               2671 IGLITATGGGCACATETAATATCHTCAGCTCTTTTTTTTTGGATATAAAATGTGCAGATGGCA 2730
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     27/1 ACTIVITIONATION TANGECACTIGAAATGITAGICATITATITATACAAGATIG 2820
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                287) AAAATOTTOTOTAAATOOTAAATTIAAAAAAFTATAAAAAAATOOTOOTOOTOOTOOTAAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      2881 TAAAATTGCTGTGTGTTATGGATAGTAAGAATGGGGCTAGAGTGGGAAGCCTGATAACGC 2940
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 2941 AGGCCTGT/TGACTAGCCT/CTT/TGTAGCATATAGGTGATGT/TGCT/CTTGT/TTT 3000
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            2911 AGGCCTGTCTGACTACTTTGCCTTCTTTTGTAGGATATAGGTGATGTTTGCTCTTGTTTT 2970
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       4001 TATTAATTIATATGTATATTTTTTTTTTAAATGTAAACACCCTTAGAAAATGTGTCCTA 3060
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        0061 ICTATCTTCCAAATGCAATTTGATTGACTGCCCATTCACCAAAAITATCCTGAACTCTTC 3120
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        (1.2.) I DOAAAAA I GGATATTAGAAA I I AGAAAAAATTACTAATTTTACACATTAGATTTT 3180
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           3240 ALLITACIALIGGAATCIGALAGUGTGTGTTGTTATAAAATTTTGCTTTTAAAA 3240
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              4241 AATAAAAGTTGGAAGCAAAGTATAACCALAIGATACIATCATACTACTACTGAAACAGATTTC 3300
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         12.1. AATAAAANOTIGGAAQCAAAGTATAACCATATGATACTATCATACTACTGAAACAGATTTC 3270
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AANSi241 standard; (DNA; 4579 BP;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Probe for retinoblastoma gene.
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141 CAGGCTIGAGITIGAAGAAAAAGAAGCIGAIIIIAQIGCAITAIGIGAGAATIAAA 200
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   201 GATANNAGATNATGTNAKAKAKANTTIGKTTAANTTIGKGAAAARITTOTIGTIGTIGT 260
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  261 YGGAGYATTGGGAGGYTTATATTGAAAAGAAAAGGAAGGGAAGGGAAGGGAAGGGAAGTGTGTGTTTAT 320
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     ostebsarboma, fibrosarboma, soft tissuc satuema, small cell sarcoma, esp. of the lung, melanoma and mammary tumours.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           501 GGAAAAGAATGTGAATTTATATATIGACACAAQGGAGGAGTGGAT------
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     25; Indels 180,
                                                                                                                                                                                                                                                                                                                                                                                                                                                      Query Match 91.6%; Score 3094; DB 9; Length 4579; Best Local Similarity 94.2%; Pred. No. 0; Matches 3329, Conservative 0, Mismatches 25; Indels 180
                                                                                                                                                                                                                                                                           Detecting pre-disposition to develop—using retinoblastoma gene probes to detect defects in the retinoblastoma.
                                                                                                                                                                                                                                                                                                                                                          The probe can be used to detect tumour with an Rb detect eq
                                                                                                                                                                                                                                                                                                                                                                                                                       Sequence 4579 BP; 1477 A; 843 C; 808 G; 1451 I; 0 other;
                                                                                                                                                                                                            Fung YKT, T'Ang A, Murphree LA, Benedict WF;
                                                                                                                                                                              (CLAY-) CLAYTON FOUNDATION FOR RESEARCH
               Probe; retinoblastoma; tumour; ss
                                                                                                                                                                                                                                                                                                                           Claim 14; Page 17; 32pp; English.
                                                                                                                                             87GB-C011646.
                                                                                                              88HP-0304900
                                                                                                                                                                                                                                             WPI; 1988-33809/48.
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<u>ج</u> :	15.24	AGATTCACCTTAATTGATCTTATTAAACAATCAAAAGAACGAAAAAAAA	- or

2647 2697 1978 2183 2303 2577 1859 TGCAAATGCAGAGACACAAGCAACCTCAGCCTTCCAGACCAGAGAAGCCATTGAAATCTAC 1918 1884 GCACACCCTGCAGAATGAGTATGAACTCATGAGAGACAGGCATTTGGAGGAAATTATGAT 1943 2219 AGAAGAGGAGTATGATTATATATATAGTGTTCTA1AACTCGGTCTTCATGCTGGAAGACTGAA 2278 2304 GACTCCAAGATCAAGAATCTTAGTATCAATTGGTGAATCATTGGGGACTTCTGAGAAGTT 2363 2424 AAGCAACCCTCCTAAACCACTGAAAAACTTACGCTTTTGATTTTGAAGGATGAAGG 2483 1824 TIGIGAACGCCTICTGTCTGAGCACCCAGAATTAGAACATATCATCTGGACCTTTTTCCA 1883 2698 TYCTACTCGAACACGAATGCAAAAGCAGAAALGAATGATAGGATGGATGGATGGATAGATAGAGAA 2757 1679 AGATTCACCTTTATTTGATCTTATTAAACAAFCAAAGGACGAGAAGGACCAACTGATCA 1748 2364 CCAGAAAATAAATCAGATGGTATGTAACAGCGACCGTGTGCTCAAAAGAAGTGCTGAAGG 2484 AGATGGAAGTAAACATCTGGCAGGAGAGTGCCAAATTTTGAGGAGAAACTGGGAGAAATGAG 2544 TTCTACTCGAACACGAATGCAAAAGCAGAAAATGAATGATAGCATGGATACCTCAAACAA 1764 CTCTCTTTCACTGTTTTATAAAAAGTGTATCGGCTAGCCTATCGGGTAACCT 1584 CCTTGAATCTGCTTGTCTTAATCTTGCTGGGGAATAATCACACAGAGATA 1739 CCTTGAATCIGCTTGTCTTAATCTTGCTGCGGAATAATCACACIGCAGAATAT 1644 GTATCTTCTCCTGTAAGATCTCCAAAGAAAAAAGGTTCAACTACGCGTGTAAATTCTAC 1704 TGCAAATGCAGAGACACAAGCAAGCTCAGGCCTTGCAGAGCCAAAGCGALTGAAATCTAG 1944 GTGTTPCPTGTATGGGATATGGAAAGTGAAATTATAGAGCTTAAATTGAAAAFAYTFCT 2099 CHCPTPCCATGTATGGGATATGGAAGAGTGAAGATATAGAACTTGAAATTGAAAATGCT 2159 AACAGCATACAAGGATCTTCCTCATGCTCTTCAGGAGGACTTCAAAGGTCTTTTCATCAA AACAAATATITITIGCAGTATGGTFGGAGGGGGGGGGTAGGTFGTGAGATACGTGAGAT 2244 TATTTCACCCTGAAGAGTCCATATAAAATTTCAGAAGGTCTGCCAACACAAAAAT 2518 CCAGAAAATAAATCAGATGGTATGTAACAGGGACCGTGTGCTCTAAAGAAGTGTTGAAGG 2064 AGAAGAGGAGTATGATTGTATTATTAGTATTGTTATAAGTGGGTGTTGATGCAGAGAGTGAA 2124 . ପ୍ର ••• pp qq ò qq qq qq ò 9 ò ô q ô ò q à qq ò q ò q ò ç ò 습 Ω 90 ò q ò qq δ ò ò

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Modified retinoblastoma tumour suppressor, RTSP protein: Gance therapy:
                    2384 ACTEGAAATGTAGTCATTGTTATTATAGATTGAAAATCTIGTGTAAATCCTGCCA 2843
                                                                                                                                                                                                                                                                                                   2998 ITTAAAAAGIIGTAGCAGATIGTTTOOTOTTOOAAGTAAAATTGOTGTGGTTATGGAT 3057
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2F44 FCTCLCACAGAFGTGACTGTATAACTTTCCCAGGTTCTGTTTATGGCCACATTTAATATG 2723
                                                                                 2/24 TICAGCIPTITITICFGGATAFAAATGTGCAGAFGCAATFGFFFGGGTGAFFCCTAAGGC 2783
                                                                                                                                                                                                                2538 ACTIGAAAICETAGICATIGETATETATACAAGAFFGAAAAFCTEGEGEAAAFCCAGCA 2997
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                                                                                                                                                                                                                                                                                                                                            29:11 - ACTAARAA BROOCETAAAARROAAA BOTTOATAARAAGGAAGGOOTTOTTOTTAATAAGTTOOPE
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7, 2694
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This arquamer enoughs a modified retinoblastoms tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting collular proliferation, when coadministered with a p53 protein. The kTSPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RTSPs have a breader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             108 GPAGGAPAGPAGPAGPAGPAGPPGGTGGGTGAGGCTTGAGTTTGAAGAAGAAGAAGA 167
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             228 TIGGTTAACTIGGGAGAAGITICAICIGGGAIGGAGIAITGGGAGGITAIAIGAAA 287
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          288 GAAAAAGGAACTGTGGGGAATCTGTATGTTTTTTTGGAGGTGACGACGTGAGATGAGATGTG 347
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 348 GITCACTITIACIGAGCIACAGAAAAACAIAGAAAIGAGIGIGGGGAAAAATIGITTAACIT 407
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    249 GTTCACTTTTACTGAGCTACAGAAAACATAGAAATCAGTGCCATAAATTCTTTTACTT 3U8
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           408 ACTABABGABAPIGATACCAGIACCABAGIIGAIAAFGCIAIGICAAGAACTGAAGAA 467
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   309 ACTAAAAGAAATIGATACCAGTACCAAAGIIGAIAATGCIAIGICAAGACIGIIGAAGAA 468
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        468 GTATGATGTATTGCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTTATATTTT 527
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          4) Indels 177; daps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     189 GAAAAAGAAATGIGGGAAATCIGIAFCIITAIIGAAGAAGIIGAAGCIAGAIGAGAIGIC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              91.1%; Score 3076.6; DB 19; Length 3455; 94.7%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  528 GAMAMAMMAGGAGITGGATGGTG------
                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 3455 RP; 1153 A; 631 C; 627 G; 1044 I; 0 other;
                                                                                                                                                                                                                                                           inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  0; Mismatches
                                                                                                                                                                                                                                                                                                Claim 22; Page 142-147; 249pp; English.
                                                                                                                                       Xu H, Zhou Y;
                                                                            (BAYU ) BAYLOR COLLEGE MEDICINE
                                                                                                                                                                                                                                                                                                                                                                                                                                       activity than wild type RTSPs.
                                     97US-0038118
98WO-US03041
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Best Local Similarity 94.74
Matches 3256; Conservative
                                                                                               UNIV TEXAS SYSTEM
                                                                                                                                                                          WPI; 1998-480788/41.
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В
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                                                                                                                                       Benedict WF,
19-FEB-1998;
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	CCYALGAITYTGAAIGIGCITAAITTAAAAGCITTGATTTTAYAAGIGAIGGAAG 	1430 1508
	III I I ALCAAAGGAGAAGGGAATTI GACAAGAAATGATAAAAGATT LAGAAGGALGTGA 	1490 1568
~ ~	AYARCMANCATGRAATCO TEGATGRETECTCAGATTCACCTTATTTGATCTTATTAA 	1550 1628
	N'AAL'AAAGAAN'O AGAAGAYCAACTGATGAACTTGAATCTGGTTGTGCTCTTAATGT 	1610 1688
611	POTECTO AGAALAA PARACIONAGA AGA ALGI ALCHTIOCO GLAAGATO GGAAA TOTTO TOTTO AGAALAATGACTOS AGAGAGATATGATOTTTO GGAAA	1670 1748

1671 GAAAAAAGGIICAACIACGGGGIGIAAALICIA GAAAALGCAGAGACACAAGAACTTC 1730 1731 AGCCTTCCAGACCCAGAAGCCALTGAAATCTACTTCTTCTTCACTTTTTALAAAAAAAT 1790 1791 GTATCGGCTAGCCTATC1CCGGCTAAATACACTT1G1GAACGCCTC1G1G1GTGACCACTT185u 1911 CATGAGAGAGGATTTGGACCAAATTATGALGTLCCALGTALGGAATALAGAAGT 1970 2109 TGTTCAGGAGATTCAAACGIGTTTIGAFCAAAGAGAGGAGTALGAILCIALTALAGT 2168 2151 CAGGCCCCTACCTTGTCACAAAACCTCACATTGCTGAAAGGCTTACAAGTTTGCTAG 2210 2211 ITCACCCTIACGGATICCIGGAGGGAAVAICIAFALIICAN CCIGAAGAGICCATATAA 2270 2271 AATTTCAGAAGGTCTGCCAACAACAAAATGAATTCGAAGAATCAAGAATCLIAGIATC 2330 2511 GEGGAAATTEGAGGAGAAACEGGGAGAAIGACTICTACTEGAACAGGAAIGEAAAAGCA 2570 2589 GTGCAAATTTGAGCAGAAATTGGCAGAAATGACTTGTACTGGAAGAAGGAATGCAAAAGGA 2648 2631 IGGI GGACACTOTOTACACPI CI GGATTOATTOTO TOTOAOAGA IO FONTOTALAAOTT - 2690 2709 TGGTGGACACTGTGTACACCTCTGGATTCATTCATCATCATCACACATGTGACTGTATAACTT 2768 2691 TOCCAGGITCIGITIALGGOORACHHAAJALOHOAGOTOTIILHOOGAAAAAA 2750 1929 AGAATTAGAACATATCATCIGGACCCTITICMAGMACACHGGAGAATGAGTATGAAMT 1988 2649 GAAAATGAATGATAGCATGGAFACCTCAAAGAAGGAGAGAAATGAGGATGTGTGTGTGTGT 2708 2229 CAGGCCCCTACCTTGTCACAATACCTCACATACTCCAAAGCCTTATAAAGTTCCTAG 2451 ACTACOCHTIGATATIGAAGGAICAGAIGAAGGAGAIGGAAGTAAAGAICIGGAAGA 2091 ATTCTATAACTCGGTCTFCATGCAGAGACTGAAAAQAAATATTTGCAGTATGCTTTCCAC 1989 CATGAGAGAGAGCATTTGGACCAAATTATGATGTGTTCCATGTATGGATGTGTATGAAAAT 1971 GAAGAATATAGACCITAAALICAAAALIGIAACAGAAGALATAGALALIGALGA 2031 TGTTCAGGAGACATTCAAACGIGIII110ATCAAAGAAGAGGAGTATGATATATATATATATAT 2571 GAAAATGAATGAIAGCATGGATACCTCAAACAAGGAAGAGAAATGAGGALCTCAGGACT <u>a</u> $^{\circ}$ g $^{\circ}$ 3 ò ò qq 5 9 ô 9 $\overset{\circ}{\circ}$ qq ò a Ś q $\dot{\circ}$ qq ò qq ò qq õ q ò a े <u>a</u> õ q 3

2751 TGCAGATGCAATTGTTTGGGTGATTCCTAAGGCACTTGAAATGTTAGTCATTGTTATTTA 2810

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                                                                                 28.29 TGCAGATGCAATTGTTTGGGTGATTCCTAAGCCACTTGAAATGTTAGTCATTGTTATTA 2888
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	36		9.92	2995	16	AAQ86 198	Human Rb110 cDNA.
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This acquence encodes a modified retinoblastoma tumous suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting cerilular prollieration, when condministered with a pSP protein. The FTSPs can be used for treating diseases characterised by abnormal cellular prollieration, particularly cancers. The RTSPs have a broader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             361 AĞAĞTGILIMAAGAAGTATGATGITTIĞITTIĞÇAĞTÇITLIĞAĞCAAATTGGAAAGGAÇATGI 420
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 121 PGGGGGGGGCTCTCGTCGTCGGCTTGGGTTTGAGAAGAAGAAGAAGAACCTGATTTTTACT 180
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                                                                                                                                                                                                                                                                                                                                  Sequence 3461 BP; 1141 A; 675 C; 627 G; 1018 T; 0 other;
                                                                                      inhibiting cellular proliteration, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                          0; Mismatches
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TITTELLITTE	CTGTCTGAGYACCCAGAATTAGAACATGTGGACCTTTTCCAGACACTGTGTAG 	AATGACHATGACHOOATGAGACAGOCALTICOACCAAATTATGAGGGGGCGCAAGTATTATTATTATGAGGGGGGGG	OOFATATIOFAAAGTGAAGAATATAGACCTTAAATTCAAAATGTAGTAGGAGGGTAGAAG 	GATCTTCCTCATGCTGTTCAGGAGACATTCAAACGTGTTTTGATCAAAGAGAGGGGTGTTTTT 	GALFOLALIAIAGIALICTATAARUGGICTICAIGCAGAGGCIGAAAAAAATATITTG TITTELLITTILITTILITTILITTILITTILI GATTCIATAIAGTATTCTAFAACTGGGCTCAAGAGGAAAAAAATATTG	PAGIALOTTITCACTAGOPOPOLAGOTIGICACAATACCTCACATICGICGAAGCCT FILLELLILLITELLILLITTITLITITLITITLITITLI	TACAACTTTCCTAGTTCACCCTACGGATTCCTGGAGGGAACATCTATATTTCACCCCTG	ANGAGICCALA LAAAAH HEYAGAAGICI GCCAACACCAACAAAA IGACI CCAAGATCA TITLI TITLI ANGAGATCA	AGAATCTTACTATCAATTGTBAATCATTCGGACTTCTGAGAAGTTCCAGAAATTAATTTTTTTT	PAGATOSTATSTAAPNGTGAPGGTGAAAAGAAGIGGGAAAGGAAGGAAGGAAGGGTGGTGAAGGAAG	AAACCACCAAAAAACTACCCTTCATATICAACCATCACAGCAACAACAAAAAAAAAA	CATCHCCAODAGAGECAAATTICAGGAGAAACTGGCAGAAATGACTECTACTGGAGAA 	GGAATOCAAAAGAAGAAATGATGATAGATAGATACCTCAAACAAGAAGAAATGA TITTITITITITITITITITITITITITITITITITIT	OBARCIPAORACCHOSTORACACTOTORACICHORATICATICHCHCACACAGTG TELETELLETELLETELLETELLETELLETELLETE	EGACT GRAFARGE FERGARDE FELGE FERBECKERA FELGARIAT AND TOTAL CHILLER FELGER FELGER FELGER FELGER FELGARIAT AND TOTAL SELECT FERBECKER FERBECKER FELGARIATE FELGARIAT F	GTGBATALAAAATGTGCAGATGTTTGGGTGATTCCTAAGCCACTGAAATGTTA - - - - - - - - - - - - - - - - - - -	GPPATIGLIALITALACAAVAHGAAAAPCTIGBGTAAATGCTGCCAFFTAAAAGTTGT 	ASTACATECTETECAAAGTAAATTGCTGTGCTTTATGGATASTAAGAATGCCCTTTTTTTTTT
38.	1921	1881	2041	2101 2101	2161	2221	2281	2 14 1	2401	2461	25.21	2581 2581	2641	2701 2701	276.1	2#21 2821	2881 2881	2941
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Modified retinoblasioma tumour suppressor; RISP protein; cancer therapy; cellular proliferation inhibitor; ss.
                                                                                                               3121 AACACCCTTAGAAAAIGTGCTATCTATCTATCCAAATGCAATTTGATTGATTGACTCTT 4180
                                                                                                                                             3181 CACCAAAATTATCCTGAACTCTTCTGCAAAAATGGATATTATTAGAAATTAGAAAAAA 4240
                                                                                                                                                                                                                             3061 ATAGGTGATGTTTGCTCTTGTTTTATTATTTATATGTATATTTTATTTTAATTTAACATG 3120
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2941 AGCAGATICTFTCCTCTFCCAAAGTAAAAFGTGTGTCTFTAFGAALAGTAAGAAFGCC 3000
                  3061 ATAGGTGATGTTTGCTGTTTTTTALTAALTTALGTALATTTTTTTTTAALTAAGTG
                                                                                                                                                        Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                               3421 CITCATCCAACTTATGLILLTAAATGAGGATLALLGALAGL 3461
                                                                                                                                                                                                                                                                                                                           Modified retinoblastoma tumour suppressor gene.
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                                                                                                                                                                                                                                                                                                                                                                                      AAV58440 standard; DNA; 3555 HP.
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(TEXA ) UNIV TEXAS SYSTEM.
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This sequence encodes a modified relinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting relinial profileration, when conduintstered with a p33 protein. The RISPs of the used for treating diseases characterised by abnormal collular. proliferation, particularly cancers. The RTSPs have a broader spectrum of FITTER FOR THE PROPERTY OF THE 268 GAGCIA/NGAAAAACAIAGAAAICAGIGCAIAAAIICIIIIAACIIAGIAAAAAAAIT 327 241 GAGAAAGITICAICIGIGGAIGGAGIATIGGGAGGITAIAIAITGAAAAGAAAAAGGAACIG 300 -----GGTCGACCTAGATGAGATGTCGTTCACTTTTACT 267 (5) GAGCTACAGAAAACAYAGAAATCAGTIGTGCATAAATTCTTTAACTTAACTAAAAGAAATT 420 328 GATAGGAGTAGGAAAGTTGATAATGCTAATGAGAGTGTTGAAGAGTATGATGATGTTG 387 121 GATACCAGIACCAAAGTIGAIAAIGTIAIGICAAGACTGITGAAGAAGTATGAIGIAITG 480 388 LITEGRALICTTCAGCAAATTGGAAAGGACATGTGAAACTTATATTTTGACACAAAACCCAGC 447 448 ASTICGAIAICIACIGAAAIAAATTOTGTATIGGGFGATAAAAGIIIGIIGGAICACAIIT 507 SER FITALITAKUTAAAGGGGAAGTATTACAAATGGAAGATGTGGTGATTTCATTTCAGTTA 567 6. L TIATTAGCTAAAGGGGAAAGTATTACAAATGGAAGATGATCTGGTGATTTCATTTCAGTTA 660 568 AIGCIAIGIGICCTTGACTATTTTATTTAAACTCTCACCTCCCATGTTGCTCAAGAACCA 627 628 INTANANCAGGIGITATACCATTANGGIICAGGIGGAACAGGGGGGGGGGGAACAAC 687 | RK | AGGAGTICCACOGATAGCAAAAGAACTAGAAATGATACAAGAATTATTGAAGTTCTCTGT | 747 748 AAAGAACA (GAATGTAATATAGATGGIGAAAAATGTTTFATTTCAAAAATTTTTATAGCT 807 93; Gaps Score 3354.8; DB 19; Length 3555; 2; indels Sequence 3555 BP; 1171 A; 684 C; 653 G; 1047 T; 0 other; 0; Mismatches Pred. No. 0, Disclosure: Page 121-126; 249pp; English. activity than wild type RTSPs. . 86.96 Similarity 97.3%; Matches 3459; Conservative ----- \$5.7 ponery Match --- 987 Local 3 5 3 3 3 3 Ś <u>a</u> ŝ 2 ó Ξ 3 = ŝ 5 Š 9

CCCAGAATTAGAACAT 1947 	200	AGUGAAGAATATAGAC 2067 	TGCTGTTCAGGAGACA 2127 	AGTATTCIAIAACICG 2187 	CACCAGGGGGGTAGC 2247 	TAGTTCACCCTTACGG 2307 FEH HITTELLIT FAGT FCACCCTTACGG 2400	TAAAATTEAGAAGGT 2367 	ATCAATTGGTGAATCA 2427 	248 258	AAAACIAGGIIIGAI 2547 	260	256 276	272	CHTHCCAGGHPCTGF 2787 	ATGTGCAGATGCAATT 2847 	TTATACAAGATTGAAA 2907 	UCCICITCCAAAGTAA 2967 HIHIIIIHIII TCCTCTTCCAAAGTAA 3060
ATACACTITGIGAACGCCTTCTGTCTGAGCACCCAGAATTAGAACA 	FCATCTGGACCCTTTTCCAGGACACCCTGCAGAATGAGTATGAACTCATGAGAGACAGG FILLELLELLELLELLELLELLELLELLELLELLELLELLE	CATHOGACCAAATTALGAIGIG HCCAIGTAIGCAAAGCAAAGGGAAGGATATAGC 	TAAATTGAAAATGATGTAAGATAGAAGATGTTGGTGATGTGGGGGG	TPCAAACGEGTTTTGAFCAAAGAAGAGAGTAFGATTCTATTATAGTATTCTATAACTCG 	GLCTICA EGYAGACACTIGAAAGAAATALI FIGGAGIATGCTICCACCAGGGCCCTAGC 	TEGECACGAATACCECACATECECEGAAGCCETACAAGTITCCETAGITECACCGTACGG 	ACA FOLATATTICACCOGIGAAGAGICCATATAAATT 	CHOPPAACACPAACAAAAHGAPPCAAGAHCAAGAAFCHTAGHTHHHHHHHHH THEFFHHHHHHHHHHHHHHHHHHHHHHH	TOGGGACTTCTGACAAGTTCCAGAAAATAAATCAGATGGTATGTAACAGGGACGGTGTG 	CTCAAAASAAKTOCTGAAGGAAGCACCTGTAAACCACTGAAAAAALAAGCTTGAT 	TGAAGGATCAGATGAAGCAAGGAAGGAAGATCTCCCAGGACACCTCCAAATTTCAG TTTTTTTTTT	AAATGACTECTACTCGAACAGGAATGCAAAAGCAGAAATGATGAT 	CAAACAABGAAGAAATGAGGATGTCAGGA 	GTACACTICTORA FECATIGICAL CACAGA EGIGACIGTATA ACTITICOCAGOTICOGO ELLELLELLE LELLE LEL GTACACTICTOGA LECATIGICA PETCAGA A LA GEGACTATA ACTITICACAGOTT COG	TAATAFCTFCAGCTCTTTTTGTGGATATAAA	FORGEGATECTAARCA/TEGAAATGTTAGTCATTGTTATTATACAAGATTGAAA 	A POTTULI OLAAA LOCI GCOATII AAAAAGII GIRAGGAGAI I GIRTII OCIOTI I COAAAGIRAA 1114 - 1114 1114 1114 1114 1114 1114 1114 1114 1114 1114 1114 1114 1114 1114 1114 ABOTEGIO STAAAROOT GOGALTITAAAAAGIT GIRAGCAGATTOSTI I COTOTI EGGAAAGITAA
TATOTOGGOTAAATACACTT 	ATCATCTGGACCC }	CALLIGGACCAAA 	CTTAAATTCAAAA 	TTCAAACGTGTTT 	GICTICATOCAGA 	TTGTCACCAATAC 	ATTO TGGAGGGAACA FOLLATATT 	CHOCCAACACCAA UTUUTUUTU CTGCCAACACCAA	TTCGGGACTTCTG 	CTCAAAAGAAGTG 	ALTGAAGGATGAG TITTTTTTTTT	GAGAAACIGGGAGAAAIGACIICI HIIIIIIIIIIIIIIIII GAGAAACIGGGAGAAAIGACIICII	AGCATGGATACCT 	GTACACCTCTGGA TITLITITITI GTACACCTCTGGA	ITATGGGCGACATT	GITTGGGTGATTC	ATCTTGTGTAAAT
уу 1888 эь 1981	лу 1948 ф 2041	27 ZOOR 25 ZIOI	27 - 2068 35 - 2161	27 2128 35 2221	x -	27 2248 35 2341	2y 2,408 do 2401	27 2368 de 2461	27 2428 35 2521	2) 2488 do 2581	25.48 bb 2641	29 2608 do 2701	27 2668 do 2761	JY 2728 th 2821	27 2788 tb 2881	28 2848 (b) 2941	29 2908 ob 4001

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                                                                                                                                                                                                                   2968 AATTGCTGTGTTTATGGATAGTAAAAATGGCCCTAGAGTGGCAGTCCTGATAACCTAG 4027
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Minimal promoter; tetracycline responsive expression vector; TREV; transcriptional transactivation domain; TTD; tetracycline repressor protein; TFP; tetracycline operator; production; stable cell line; production; stable cell line; protein ground: suppressor protein; treatment; cancer; ss.
                                                                                 3088 TAATTTATATGTATGTTTTTTAATTTTAAGATGAAGAGGTTAGAAAALGTGTGTTATGT
                                                                                                                         3148 ATCTTCCAAATGCAATTTGATTGACTGCCATTCACCAAAATTATGCTGAAGTCTTGTG
                                         3028 CCTGTCTGACTACTTTGCCTTCTTTTGTAGATATAGGTGATGTTGCTCTTGTTTAL
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P-PSDB; AAW71354.

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New retracycline responsive expression vectors - used for the tightly controlled expression of genes, such as tumour suppressor genes for freating cancers
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Disclosure: Pages 145-150: 190pp: English.

The present sequence appears in the specification, which describes a terracycline responsive expression vector (TRFV), which contains a sequence encoding a tusion protein comprising a transcriptional transactivation domain (TIE) pretainely attached to a tetracycline repressor protein (TRF), the first sequence operatively positioned downstream of a bosoncer. The vector also contains a cloning site operatively positioned downstream of a based promoter comprising a terracycline operator. The TREVS can be used to produce stable cell lines in which gene expression is Lightly regulated by lefracycline. They can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers.

sequence 3555 BP; 1171 A; 684 C; 653 G; 1047 I; 0 other;

180 233 360 507 600 HITTELLETTELlettel 6.1. QAACG???GGGAGGGPTGAGGAGGAGTATTPTBAAGAAGAAGAAGAAGAAGAGAGGGG7.0 121 POGGAGGACCEGONTOTOGICANAGAGTITGAGATTGAAGAAANAGAAANGAANOTGATITIAGI 180 18] SOATIATGICASAAATTAAAGATASSAGATPATGIPAGAGAGAGAGGITAAFITGG 240 258 GAGGIACAGAAAAACAIAGAAAIGAGIGIGCAIAAAIIGIIIAACIIACIAAAAGAAAII 327 328 GATACCAGTACCAAAGTHGATAATGTTAAGAGAGTTGTTGAAGAAGTATGATGTTAG 387 388 TTTGCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATATTTGACACAACCCAGC 447 5/48 11A11AGCTAAAGGGGAAGTATTACAAATGGAAGATGATCTGGTGATTTCATTTCAGTTA 567 568 ATGCTATGTCCTTGACTATTTTATAAACTCTCAGCTCCCATGTTGCTCAAAGAACCA 627 181 WAITATGICAGAAATTAAAGATACCAGAICATGICAGAGAGAGAGCTIGGIT-----121 Prodaddadergerererereaderrigadrimgaagaacagaagarerrimmer -----GGTCGACCTAGATGAGATGTCGTTCACTTTACT 30) TÖĞĞAATÇIĞTATÇITTATTĞĞAĞCAĞTTGAĞCTAĞATĞAĞATĞIÇĞTTTÇAÇTTTAĞT 448 ASTICGATATCTACTGAAATAAATTCTGCATTGGTGCTAAAAAGTTTCTTGGAGATCACAITT 541 AGTICGAIAICIAGIGAAAIAAAIICIGCAIIGGIGCIAAAAAGTITCIIGGAICACAIIT 96.9%; Score 3354.8; DB 19; Length 3555; 2) Indels Pred. No. 0; 97.38: Congressive Similarity Matches 459 Querry March 7 3 4 Ś 5 <u>-</u>2 5 3 Š $\bar{\Xi}$ ā

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1648 CGAGAAAGGACCAACTGAFCACTTGAATCTGTCTGTTGTTAATGTTTCCTCTCAGAAT 1707
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                            628 TATAAAAÇAGÇIGTTATAZOPATTAALGGITTPAÇETÇGAAÇAGÇAGGÇGAGGLGAGA
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	1767 1860	AATCACACTGCAGCAGATATGTATCTTTCTCCTGTAAGATCTCCAAAGAAAAAGTTCA 	1708	5 3

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hEST2; telomerase; catalytic subunit; reverse transcriptase; lite-span; retinoblastoma; p53; tumour suppressor; inhibitor; arteriosclerosis; prollferation; immortal; tumour therapy; macular dequeration, activator;
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2881 TTATGGCCACATTAATATCTTCAGCTCTTTTGTGGATATAAAATGTGCAGATGCAATT 2940
                                                                                                     2848 GTTTGGGTGATTCCTAAGCCACTTGAAATGTTAGTCALTGTTALTALACAAGATTGAAA
                                                          2941 GITIGGGIGATICCIAAGCCACTIGAAATGITAGICATIGITATITATACAAGAITGAAA
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17-FEB-1999;
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treat conditions related to (premature) agains, e.g. macular degeneration and arteriosclerosis. The cells can also be used to replace tumour cell lines in vitro and for studies or biochemical and physiological aspects of growth and differentiation. Iong lived (immortal) cells could also be of use in the production of normal or genetically engineered.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              e.g. the number of mitoric divisions, of a cell. The method relies on activation of a telometrase activity and inhibition of one of both of a retinoblastoms (Pb)/INK4 pathway or a p53 pathway. Phosphorylation of Rb by cyclin dependent Kinascs, odk4 and cdk6, releases the cells into the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         division cycle. Binding of TMK4 family members, e.g. the tumour sittesset planks. Edities thase article and results in grach arrest. Be inactivated an selectively and recersibly inactivate an PP TMK4 perlang reportedly, a. Profitting perlang. The enceptation of the conspication of the constraint and can also be used in the methods. Other molecules which can be used include cdk4 or cdk6 mutants. In particular, a cdk4 mutant is one which
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                The invention concerns methods and readents for extending the life span.
                                                                                                                                                                                                                                                                                                           New method for increasing the proliferative capacity of cell lines comprises administering agents reversibly activating telomerase and interestibly inactiviting Ph/INM4 and/or p53 pathways useful
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        subsequently of use in pharmaceutical and cosmette preparations used to
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Additional constructs include a papilloma virus E7 protein, or other
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Jisim 5; Page 121-123; 123pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     in treating age related diseases
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( TENE ) GENETICA INC
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122 **SGAGGAGGIGGCIGTGTGGFGAGGCTTGAGGAAACAGAAGAAGCTGATTTTACTG 181 43 + ANAAANTTTOATOTOTOTOGAGGTATTGGGAGGTTATATTGAAAASAAAAAGGAACTGT 432 ------GGIGGACCTAGATGAGATGTGGTTGACTTTACTG 268 269 AGCTACAGAAAAACATAGAAATCAGTGCATAAATTCTTTAACTTACTAAAAATTG 328 93; Gaps 96.9%; Score 3353.8; DB 21; Length 4839; 2; Indels Sequence 4834 RP; 1534 A, 902 C, 880 G, 1523 I, 0 other, Pred. No. 0; 0; Mismatches 97.38; Conservative Similarity Matches 3458; Swory Match Ś â 5 Ē

1409 GCAGAAGTACATCTCAGAAATCTTGAAACAGATTTGTCCCATGCCATGGA 1468

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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        facilitate the development of screening assays to evaluate the potential
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       designated RD. Androgen receptor to activator proteins from the prosent invention can be used in screening assays to identify candidate pharmaceutical molecules for the ability to promote or inhibit the interaction of androgen receptors and androgen responsive enemons to modulate androgen cactivity. The identification and characterisation of androgen receptor co-activators such as those of the invention will
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Novel androgen receptor-associated proteins used to detect androgenic
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   214 TOGAGGAFOTT GOG TOTT GOTT GAGT TEGAGAAGAAGAAGAAGAAGAAGAAGAAGTIGA TTPT AGTIG
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                                                                                             Human: androyen receptor coactivator; ARA54; ARA55, ARA24, detection,
                                                                                                                       Rb; androgenic; antiandrogenic; identification; prostate cancer; ss.
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                                              Frinan androgen receptor coactivator Rb encoding china SEQ 15 NG 7
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           or antiandrogenic activity in serrening assays for candidate pharmaceutical molecules which promote or inhibit the activity
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               ethicacy of drugs in the treatment of prostate cancer.
                                                                                                                                                                                                                                                                                                                      /note- "androgen receptor coactivator"
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-----GGTCGACCTAGATGAGATGTCGTTCACTTTTACTG 268
                                                                 433 GGGGAALFLGLALFTTTATTGGAGGAGLIGAGCLASAIGAGAIGFGGLIGAGLITTACTG 492
                                                                                                                                      269 ACCTACAGAAAACATAGAAATCAGTGTCCCATAAATLCTTTAACTTACTAAAAAAAAATLG 328
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3313 AATTTATATGTATATTTTTTTAATTTAACATGAACACCCTTAGAAAAATGTGTGCTATGTA 3372 2593 TGCCAACAACAAAAATGACTCCAAGATCAAGAATGTTAGTATCAATTGGTGAATCAT 2489 TCAAAAGAAGTGCTGAAGGAAGCAACCCTCCTAAACCATGAAAAAACTACCTTTGATA 2549 TTGAAGGATCAGATGAAGCAGATGGAAGTAAACATGTCCAGGAGAGTCCAAATTTGAAG 2609 AGAAACTGGCAGAAATGACTTCTACTGGAACAGGAATGCAAAAAGGAGAAAATGAAATAA 2833 AGAAACHGGCAGAAATGACHTCTACHGGAACAAGAAAAGGAGAAAALGAALAAA 2669-GPATGRATAPPPPAAPAARAGAAATGAGATETPAGGACETTGGETGACTG 2729 PACACCTICTICGATTICATTGTCTCTCGACACATGTCACTATAACTTTTCTCACACTTTTCTTT 2789 TATGGCCACATTTAATALCTTCAGCTCTTTTGTGGATATAAAATGTGCAAATGCAATTG 2849 TTTGGGTGATTCCTAAGCCACTGAAATGTTAGTCATTGTTATATACAAGATTGAAAA 3073 TTTGGTGATTCCTAAGCCACTTGAAALGTTAGTTGATTGTTGTTATACAAGATTGAAAA 3149 TCTTCCAAATGCAATTTGACTGGCGATTCACCAAAATTATGCTGAAATTTTGGG 3373 TCPFCCAAATGCAATFTGATTGACTGCCALICACCAAAATTATGCTGAACTTTTGCA 2653 TCCGGACTFFCFGAGAAGTFCCAGAAATAAATCAGATGGTATGTAACAGCGACGFGTGC 2909 TCTTGTGTAAATGCTGGCATTTAAAAAGTTGTAGCAGA FFGTTTGCTCTTGTTGCAAAGTAAA 3029 CIGICIGACIACITIGCCIICITITIGIAGCAIAIAGGIGAIGITICCICITITITATI 3209 AAAATGGATATTATTAGAAATTAGAAAAAAATTACTAATTTACAATTAGATTTTATTT 2969 ATTICCTOTOTTTATICGATAGTAAGAATGGCCTTAGAGTGGGAGTCCTGATAAGGCAG 3673 GATTATTGATAGT 3685 3449 GATTATTGATAGT 3461 **Ω** q qq q q οy qq ò q qq qd òλ 5 ô q qq 9 ò q qq 9 qc QΩ ò ò ò $^{\circ}$ Ś 5 ò ò $\overset{\circ}{\circ}$ ò ò ô ò

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cyrostatios dependency, antineoplastic Wilm's tumours adeporarchnoma;
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                            ABL62873 standard; DNA; 4839 BP.
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RESULT 6
               ABL62874
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The present invention describes a method (M1) for screening for an anti-neoplastic agent. The method involves exposing cells to a chemical application to be tested for anti-neoplastic activity, determining a chemical agent to be tested for anti-neoplastic activity, determining the competition of at least one gene (I) of a signification of the feat one gene (I) of a signification of a feat consistence (I) has cylostatic activity and can be used for producing a product which is the data conflicted with respect to the anti-neoplastic agent which is sufficient to convey the chemical activity and the data is sufficient to convey the chemical cannot be used in the consistence of cancer and as colon, breast, stomach, lung, thyroid, one sophageal, ovarian, kidney, prostate or pancreatic cancer, represent and Milm's tumour, infiltrating ductal cancer, infiltrating ductal cancer, squamons, papillary catching and Wilm's tumour.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          433 GGGGANTELGLATETETATEGAGGASTIGAGGTAGATGAGATGTGGTEGATTLAGIG 192
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                                               Gereening for anti neoplastic agent involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, and determining a change in expression of a gene of a signature gene set
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WPI; 2002-188264/24.
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Matches 3458; Conserve
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449 CTICGAIAICIACIGAAAIAAAIICIGCAIRSIGCIAAAAGIIICIIGGAICACAIIII S08

509 TATTAGCIAAAGGGGAAGIATPACAATGGAAGAIGA;CIGGIGATICGATILGAGIIAA. 568

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2113 ATCTGGGGCTAAATACACTTTGTGAACGCTCTGTCTGTCGGACACCCAGAATACATA 217.2 1769 CTACGCGTGTAAATTCTACTGCAAAATGCAGAGACACAAAACATCAGAATTCCAGAACT 1828 2009 ATTIGGACCAAATTATGATGTGCATGTATGGCATATGCAAAGAAATATAGACC 2068 2293 TTAAATTCAAAATCATGTAACAGGATAGAAGGATCTTCCTCATGCTGTCAGGAGAT 2352 25.33 PTCCTGGAGGAAGAPCTATATTTGACCCTGAAGAGTCGATATAAAATT FCAGAAGGTC 25.92 2369 TGCCAACCAACAAAAATGACTCCAAGATCAAGAATCTTAGTATCAATTGGTGAATCAT 2428 2713 TCAAAAGAACTGCTGAAGGAAGCCTCCTAAACCACTGAAAAAATTACGTTTCATA 2772 2773 TTGAAGGATCAGATGAAGCASATGSAASTAAACATCTCCCAGGAGGAGGAGTTCAGC 28-42 2669 GOATGGATACCECAAACAAGAGAAAATGAGGATCFCAGGACTFGCTCGACACTGTG 2728 1649 GAGAAGGACCAACTGAATCTGGATTGTGTTGTTGTTAATCTTGTTGTTGTTGTTAATA 1708 1709 ATCACACTIGCAGCAGATAIGTATGTTTCICCIGLAAGAIGTCCAAAGAAAAAAATTGAA 1768 1933 ATCACACTGCAGCAGATATGTATCTTTCTCCTGIAAGALCTGCAAAGAAAAAAAAAAAAA 1992 1829 AGAAGCCATTGAAATCTACCTCTTTCACTGTTTTATAAAAAGTGTATCGGCTAGCCT 1888 2069 TTAAATTCAAAATCATTGTAACAGCATACAAGGATCTTCCTCATGCTGTTCAGGAGATT 2128 2129 ICAAACGTGTTTGATCAAAGAAGAGGAGTATGATTGTATTATAGTATTGTATAACTCGG 2188 TCTICATGCAGAGACTGAAAACAAATATTTGCAGIACITCCAGCAGGCCCAITACCT 224B 2249 TGTGACCAATACCTCACATGCTCGAAGCCCTTACAAGTTTCCTAGTACATTCATATA 2308 2429 TCGGGACTTCTGAGAAGTTCGAGAAATAAATCAGATGGTATGTAACAGCGACGTGTGC 2488 1813 AATCCCTTGCATGCCTCTCAGATTCACTLIALLIGAL/11A11AAALAAALAAAGAACT 1872 1949 TCATCIGGACCCTITICCAGCACCCTGCAGAATGAGIATGAACTGATGAGAGAGAGAGG 2609 AGAAACTGGCAGAAATGACTTCTACTGGAACAGGAATGCAAAAQCAGAAAA GAATGATA 1993 CTACCCCTCTAAATTICTACTCCAAATGCAGAGAGAAAAAAACAACCTCAGACTTTCCAGACCC 2053 AGAAGCCATTGAAATCTACTCTCTTTCACTCTTTAAAAAGTGTATCGGTTAGCCT 2413 TCTTCATGCAGAGACTGAAAACAAATATTTTGCAGTATGCTTCCACCAGGCCCTTACCT 2473 TGTCACCAATACCTCACATTCCTCGAAGCCCTTACAAGTTTCCTAGTTCACCCTTACGCA 2309 TICCIGGAGGAAGATGIAITICACCCIGAAGAGICCATATAAAATTTCAGAAGGIC 2653 TCGGGACTTCTCAGAAGTTCTAGAAATAAATCAGATGGTATGGTAACAGCGACGTGTGC qn ò ô qq $^{\circ}$ d ò <u>q</u> ŝ qq õ d ŝ 3 ò qq ò g ó 1) P ò qq ò qq ò ć å $\overset{\circ}{\circ}$ a ŝ 3 qq ò qq ć **Q**

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Medified retinablastoma tumour suppressor; RTSP protein, cancer therapy:
                   2729 TACACCICTGGATTCATTGTCTCTCACAGATGTGACTGTATAACTTTCCCAGGTTCTGTT 2788
                                                                        2789 IAIGGGGA-AITIAAIAICIICGGCCICIIIITGIGGAIAIAAAAIGGGAAGAIGGGAAIGG 2848
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                                                                                                                                                                                                                                                                                                                   Modified retinoblastoma tumour suppressor gene
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This sequence encodes a modified retinoblastome temour suppressor protein (RYSP) of the invention. The proteins can be used for inhibiting cerlular proliferation, when coadministered with a p53 facterin. The KISPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      61 GAAPPERESSANTAPPERESPERIESPERENTERPERAGAGAGGAGGAGGAGGAGGAPAGGGAPAGGGG 120
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      4; Indels
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Taim 12; Page 17: 149, 149pp; English.
                                                                                                                                                                                                                                                                                                         (BAYU ) BAYLOR COLLEGE MEDICINE
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P-PSDB; AAW69376.
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- using genetic material corresp. to a normal
                                                                                                                                                                                                                                                                                                                                                                                                                             neoplasm. It is used to produce an antibody to the protein, contacting this with the tumour sample and detecting immune complexes as indication of the presence in the tumour sample of the protein. Whole sequence or a unique sub-region can be used. The method identifies patients lacking the defective relinchlastoma (RP) allele and thus are not at risk of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 451 IOGAJATOTANGAAAJAAATIGIGGALIGGIGCIAAAAGINICINGGALGAGALITIIA 510
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              64 OTCHRIGGIACHGINGTOGOGOGOTOTOTGAGAAGAGAGOOGAGAGAAGGAAAGGAAAGGAGGCCG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         124 GAGGAPPTGPPTFPPGTPAGGPTFGAGTTTGAAGAAAGAAGAAGAAGATTTACTGGA 183
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          119 GA-GACTIGNITATITATICAGCTIGAGITIGAAGAAACAGAAGAACCTGATITIACIGCA 177
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              238 AAAGTTTCATCTCTGGATGGAGTATTGGGAGGTTATATTGAAAAGAAAAAGGAACTG1G5 247
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 -----GGTGGAGGIAGAIGAGAIGTGGTTGAGTTTTAGTGAG 270
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          271 CTACAGAAAACATAGAAATCAGTGTCCATAAATFCTT;AACTTACTAAAAGAAATTGAT 330
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   331 ACCAGTACCAAAGTTGATAATGCTATGTCAAGAGTGTTGAAGAAGAAGTATGATGTTTTT 490
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         391 GTATTTGAGTAAATFGGAAAAGGACATGTGAATTATATTTGACACAACGGAGCAGT 450
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             478 GTAPTOTIVAG AAATTGGAAAGGAABTGTGAACTIATATGTGGACACACCAGCAGCAG
                                                                                                                                                                                                                                                                                                                                                                                                             This gene encodes a protein, the absence of which is associated with
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         4 GICALGONGONTAAAAONTHONAAAAAAAAOGOGGOAGOGOGGOGGGCGCGCGGGAA 63
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            96.0%; Score 3324.2; DB 9; Length 4597; 97.2%; Pred, No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 3; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Sequence 4597 BP; 1489 A; 839 C; 815 G; 1454 T; 0 other;
                                                                                                                                                                                                                                                                                                                                      human retinoblastoma gene or a unique sub-region
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     0; Mismatches
                                                                                                                                                                                     (WHIT-) WHITEHEAD INST BIOMED RE
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                97.28;
                                                                                                                                                                                                                                                                                                                 Diagnosis of retinoblastoma
                                                                                                                          8608-0895163.
                                                                                        87EP-0307095
                                                                                                                                                                                                                                                                                                                                                                        Disclosure; ; p; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Best Local Similarity 97.2
Matches 3452, Conservative
                                                                                                                                                                 (MASS-) MASSACHUSETS EYE
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     developing the disease.
                                                                                                                                                                                                                      Dryja TP, Friend S;
                                                                                                                                                                                                                                                       WPI; 1988-065827/10.
                                                                                                                                                                                                                                                                             P-PSDB; AAF8211
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                                                     09-MAR-1988
               EP259031-A.
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5. 48 8. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5.	5.1.2 8.6.2	571 658	6.41	6341 778	75.1 8 18	811	958	7.41 1018	991 1078	1051	1111	1171 1258	1231	1291	1351 1438	1411 1498	1471 1558	15.41
401	5 3	3 3	<u> </u>	5 G	<u> </u>	S 3	97 15b	5 3	5 4	25	5 G	75 75	421	5 3	§ 3	5 G	5 3	<u>*</u>

TCANCAATACCICACATTCCICGAAGCCITAAAGHIGGAAGHIGGAAGAATA 2397 1711 CACACTGCAGCAGTATGTATGTTTCTCCTGTAAGATGTCCAAAGAAAAGAAGTTCAACT 1770 1891 CTCCGCCTAAATACACTTTTGTGAACGCCTTCTGTCTGAGCACACAGAATTAGAACATATC 1950 2278 TTCATGCAGAGACTGAAAATATTTTGCAGTATGCTTCGAGGCCCGCTAACTTG 2337 CCIGGAGGAACATCTATATTTCACCCTCAAGAGTCCATATAAAAATTTCAGAAGGTCTG 2370 2578 AAAAGAAGTGCTGAAGGAAGCGTTGCTAAAGGACTGAAAAAAATTACGTTTGATATT 2637 2698 AAACTGGCAGAAATGACTCTCTACTCGAACACGAATGCAAAAGCAGAAAAGGAGATGATAGA 2757 1618 GGCAACTTGACAAGAGAAATGATAAAAACATTTAGAAAGATGTGAAACATGGAATGAAA 1677 1678 TOCCTTGCATGCCTCTCAGATTCACCTTTATTTGATCATTAAACAATCAAAGGAGGA 1737 2191 TTCATGCAGAGAGAGAAAATATTTAGAAATATGCAACAAGGCCCCAACTG AAGCCATTGAAATCTACCTCTCTTTCACTGTTTTATAAAAAAGTGTATCGGCTAGCCTAT 1918 AAGCCATTGAAATCTACCTCTCTTTCACTGTTTTATAAAAAAGGTATGGGCTAGCCTTT 1978 CTCCGGCTAAATACACTTTGTGAACGCCTTCTGTGAGCACCACAGAATTAGAACATATC 2131 AAACGEGTTT FGATCAAAGAGGAGTATGAT GLATLATAGTAL FCLALAAM OG DY 2251 TCACCAATACCTCACATTCCTCGAAGCCTTACAAGTTTCCTAGTTCACCTTACCGATT 2491 AAAAGAAGTGGTGAAGGAAGCAGCTGCTAAAGGATGAAAAAATTAGGTTTGATATT 2638 GAAGGATCAGATGAAGCAGATGGAAGTAAACATCTCCCAGGAGAGTCCAAATTTCAGGAG 1651 GAAGGACCAACTGATCTGATCTGCTTGTCTTAATCTTACTCTCCTCTCTAATAAT 2011 TTGGACCAAATTATGATGTTCCATGTATGGCATATGCAAAGTGAAGAATATAGACTT 2518 GGGACTTCTGAGAAGTTCCAGAAAATAAATCAGATGGTATGTAAACAGGACGTGTGCTC 2551 GAAGGATCAGATGAAGCAGATGGAAGTAAACATCTCCCAGGAGAGTCCAAATTTCAGGAG 1858 2338 2311 . • QQ a q င် 9 ć Ω Ξ. ò <u>a</u> ò q ò g ò q Š 9 Š â 3 <u>a</u> ò 9 $^{\circ}$ Q οy ò Š Q ò g a

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                         2758 ALGGALACCICAAACAAGAAGAAGAAAAIGAGGAICTCAGGACCTTGGTGACACACTCGGA 2817
                                                                                                       2341 CACCICIGGATICATIGICICACACAGIGIGACIGIAIAACITICCCAGGIICIGIITA 2790,
2671 ATGGATACTTCAAACAAGGAGAAAATGAGGATCTCAGGGCCTTGGTGGACGCTGTTTT 2730
                                                                                                                                2818 CACCICIOSALICALIGITHITHITHITHITHITHITHITHITHITHITHITH 2877
                                                                                                                                                                                                           2791 TOGGGAGATITAATATGTIGAGGTGTTTTTTTGTGGATATAAAATGTGGGAGGTGGAATTGTTT 2850
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                                                                                                                                                                                                                                                                                                                                              **** TGCIGIGCTIATGGATAGTAAGAATGGCCTAGAGTGGGAGTCCTGATAACCCAGGCCT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Retinoblastoma: cancer; detection, diagnosis; protein; neoplasm;
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A method for detecting the presence, in a tumour sample, of a protein the absence of which is associated with a neceivasm, comprises producing an antibody to the protein and then contacting the autibody with the tumour sample. Immune complexes indicate the
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                418 ACCACTACCAAACTTGATAATGCTATGTCAAGACTGTTGAAGAAGTATGTALTGTT 477
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 antibody with the tumour sample. Immune complexes indicate the presence of the protein in the sample. The method may be used in the detection and troatment of a defective human gene related to
                                                                                                                                                                                                                                                                                                                                    Diagnosing the presence of defective retineblastome alleles -
comprises comparing genetic material corresponding to a normal
human retinoblastoma with DNA from a patient.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Score 3324.2;
Pred. No. 0;
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                                                                                                                                                                                                     (MASS-) MASSACHUSETTS EYE & EAR INFIRMARY
                                                                                                                                                                                                                                                                                                                                                                                                         Example 2(2); Figure 7; 18pp; English.
                                                                                                                                                                                                                       (WHED ) WHITEHEAD INST BIOMEDICAL RES
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             cancer, in particular retinoblastoma.
Location/Qualifiers
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97.28;
                                                                                                                                                                   86US-0895163.
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P-PSDB; AAR58568.
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24.30 2098 TTGGGCCAAATTATGATGTGTGCATGTATGGCATGTGGGAAAGTGAAGAAATATGGCGT 2157 1531 GGCAACTTGACAAGAGAATGATAAAAGATTTAGAAGATGTGAAGTATGAATTATGGAA 1550 1678 Tecentidealgorereagalicacettathialethaliaaraalfaaadaacaa 1737 1651 GAAGGACCAACTGATCACCTTGATCTGCTTGTCTCTTAATCTCCTCTAAATAAT 1210 1711 CACACTGCACCAGATATGTATGTTCTCCTGTAAGATGTCCCAAAGAAAAAAAGTTTAAACT 1770 1798 CACACTICCAGCAGATATGTATGTTTCTCCTGTAAGATGTCCCAAAGAAAAAAGCTTCAACT 1857 1918 ANGCCATTGAAATCTACCTCTCTTTCACTGTTTATAAAAAAGTGTATCGGCTAGCCTAT 1977 1891 CTCCGGGTAAATACACTTTGTGAAGGCTTTGTGTGTGAGGAGGAGGAATTAGAATATATC 1950 2071 AAATTCAAAATCATTGTAACAGGATACAAGGATGTTPPPCATGGTGTTCAGGAGACATTP 2130 2131 AAACGTGTTTTGATCAAAGAAGAGGAGTATGATTGTATAATAGTATTGTATAAAATGGGTC 2190 2278 TTCATGCAGAGACTGAAAACAAATTTTGCAGTATGCTTCCAGGGCCCCTACCTTG 2447 2251 TCACCAATACCTCACATTCCTCGAAGCCCTTACAAGTTTCCTAGTTCACCTTACAGTT 2310 2338 TCACCAATACCTCACATTCCTCGAAGCCCTTACAGTTTCCTACHCACCTTACAGTT 2397 2311 CCTGGAGGAACATCTATATTTCACCCCTGAAGAGTCCATATAAAATTTCAGAAGGTCTG 2470 2551 GAAGGATCAGATGAAGGAGATGGAAGTAAACATCTCCGAGGAGAGTCCAAATTTCAGAG 2610 26.38 GAAGGATCAGATGAAGGAAGTAAAACATCTCCCAGAGAGACTCCAAATTTCAGATA 26.97 1558 GTGCTTAATTTAAAAGCCTTTGATTTTTACAAAGTGATCGAAAGTTTTATCAAAGCAGAA 1617 1831 AAGGCATTGAAATCTAGCTCTGTTTCACTGTTTTATAAAAAGGTGTATGGGCTAGGCTATGT 1890 2218 AAACGIGITITIGALGAAGAAGAGGAGIAIGAILGIAITAIAGIATIGIAIAAGIGGGIG 2277 1771 ACGCGTGTAAATTCTACTGCAAAGCAAAAW NCAAACAAAACTCAAACTTCAAAAACAAG 1591 TCCCTTGCATGGCTCTCAGATTCACCTTTAITIGAL HALLAAACAACAAGGAGGAG 2371 CCAACACCAACAAAATGACTCCAAGATCAAGAATCTTAGTATGAATTGAATTCAATTC 2491 AAAAGAAGTGGTGAAGGAAGGAAGCGTGTIAAAGGATGAAAAAAGTACGTTFGATATT 24.31 GGGACTTCTGAGAAGTTCCAGAAATAAA1CAGAIGGTATGTAACAGGGACCGTGTGCC 1978 CICCGGGTIAAATACACTTTGIGAAGGCGIICIGIGIGAGGAGGCAGAAIIAGAACAIAIG 1951 ATCTGGACCCTTTTCCAGCACACCCCTGCAGAATGAGTATGAACTCATGAGAAAAAAT 2011 THGGACCAAATTATGATGTGTTGCATGTATGGATATGGAAAGTGAAGAATATAGACTT 2191 HTGAEGRAGAGACTGAAAANATATTTGGAGTA;GCTTCCACAGGGGGCCT;ACTTG 2398 CCTGGAGGGAACATCTAFAFTTCACCCCTGAAGAGTCCATATAAAAFTTCACAAGGTCTC ò ò **Q** ò q Š 3 ŝ Q ò qq ें q ŝ q $\overset{\circ}{2}$ q δ q ò qq δ QQ οy 2 ò 2 ò U. $^{\rm Q}_{\rm Y}$ 9 ò q ò qq

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27.3. CACCICIGGATICATICICICICACAÇANGIGACINGRANIAACITITICOCAGGITICIIGITITA 2790
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                                                                                                                                                                                                                                                                                                                                                                                                                                     2851 PAGGTGATTGGTAAGGGAGTAGTGAAAFGTTAGTGATGGTAAGGATAGAAAAAA
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relinshiasterma gene Rb. Absence of mailting of the instance issue as AxA04502) predisposes an individual to retinoblastoma. To isolate We have, the human name price FH3. Isolated from a human chromosome 13 lambda phage library, was used in a chromosome walk to isolate and map 40 kb of genomic DNA surrounding the H3.8 of squence. Fragment p7H30.7R (ATCC 97500) was obtained, and was used as a probe to screen a cDNA library that had been constructed from an adenovirus 12-transformed human embryonic retinal cell inc. This provided clone F4.7R (ATCC 97387), which is northern bluts cross-reacted with a 4.7 k ATCC 97387), which is northern bluts cross-reacted with a 4.7 k transformed cell samples. Rb nucleic acids comprising the Rb osteosarroma cell samples. Rb nucleic acids comprising the Rb of ene. ChNA or a fragment of the gene, such as one of the 27 exons or 25 introns, can be used in a claimed method for detecting a deletion or point mutation in the Rb gene of a human patient. The gene can also however the synthesize Pt prigetide (see AAVUTA1) for gene can also however.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       124 GAGGACTIGOCTECTOSTO AGGCTTGAGTTTGAAGAAACAGAAGAACAGAACTGATTTTACTGCA 183
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                96; Gaps
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Query Match 96.0%; Score 3224.2; DR 20; Longth 4597; Best Local Similarity 97.2%; Pred. No. 0; Matches 3452; Conservative 0; Mismatches 3; Indels 96; Conservative 0; Mismatches 35 and 100 mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  This is the nucleic acid sequence of a cDNA of the normal human
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                                                                                                                                   Location/Qualifiers
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Best Local Similarity
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anticancer agent is used for the treatment of cancers such as breast, bladder, skin, stoment, liver, colon and cral carity. Tymphona and cukenmia. The anticancer agent induces apoptotic death of cancer cells and the Rb inhibitor increases the apoptotic inducing activity of mycolactoc ever in Rb positive cancer cells. The agent is specific to mancers in which Rb professive employing are optimally expressed and mycolactone shows very strong anticancer effort in vitro as well as in vivo.
                                                              3391 CAGAATGTAAAAGAACTTACTGATTATTTTCTTCAACCTATGTTTTTAAATGAGGA 3450
                                                                                               3418 AGCTGGAAGGAAAGTATAACCATATGALACTACTACTAGTAGAAAAGAATLFCALACCL 3477
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Human: retinoblastoma protein, Mb: cytociatic; cancer; apoptosis;
productome, antisense, breadt cancer, biadder cancer, skin can er;
stomesh cancer: Tyer cancer; coica cancer; oral cavity cancer;
Tymphoma; leukaemia; genes ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           The invention relates to an anticancer agent comprising mycolactone. Also included for is an anticancer agent comprising mycolactone and antisense inhibitors of retinoblastoma (Rb) protein expression. The
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Anticancer agent useful for treatment of cancer e.g. of skin,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 7; Indels
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Human retinoblastoma protein cDNA sequence.
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97.1%; Pred. No. 0;
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                                                                                                                                                                                                                                                                                                                                                                                                             ABK85079 standard; cDNA; 4740 BP.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          to probe can be used to detect tumour with an Rb defect egaleospreama, fibrospreama, soft lissue sarcoma, small cell sarcoma, p. of the lung, melanoma and mammary tumours.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         234
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Match 94.0%; Score 3254; Da 9; Longth 4579; Local Similarity 96.4%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Hecting pre-disposition to develop - using retinoblastoma are probes to detect defects in the retinoblastoma.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            quence 4579 HP; 1477 A; 843 C; 808 G; 1451 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            ng YKT, T'Ang A, Murphree LA, Benedict WF;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       :01 GATACCAGATCATGTCAGAGAGAGAGCTTGGTT---
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               obe, retinoblastoma; tumour; ss.
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                                                                                                                                                                                                                                                                                                                                                                      N81261 standard; cDNA; 4579 BP.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      obe for retinoblastoma gene.
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                                                                                                                                                                                                                    48 GCATTATTCATACT 3461
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ολ	1308	AGANCGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTCATATGTC 1367
qq.	1379	AGANGGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTCATATGTC 1438
. o	1368	TTTATTGGCGTCTTGAGGTGGAGGTGAATGGCGAAATATAGAAAGTATAAAAAAAA
qq	1439	TTATTGGCGTGCGCTCTTGAGGTTGTAATGGCCACATATAGCAGAAGTACATCAGAA 1498
ò :	1428	428 TCTTGATTCTGGAACAGATTTGTCTTTCCCAFGGATTCTGAATGTGCTTAAATTTAAAAGE 1487
<u>a</u>	2. 2. 2.	TCTTGATTCAGGAACAGATTGTCTLTCCCATGGALTCTGAATGTGCTTAATTTAAAAGC-1558
ć č	1488	CTTGATTTTACAAAGGATCGAAAGTTTATCAAAGCAGAAGGAACTGA AAGAGA 1547
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ŏ i	1548	AATGATAAAAGATTTAGAAAGALGTGAACALGAATGATGATGCCTTGATGATGTTT 1607
qq	1619	AATGATAAAACATITAGAACGATGTGAACATCGAATCATGGAATCCTTTGCATGGCTCPC 1678
ς c	1608	AGATTCACCTITATITGAICTIAIIAAACAAICAAAGGAACGACAGACGACGACTGATGA 1667
a	1679	AGATTCACCTTTATTTGALCTTATTAAACAATCAAAGGACCGAGAAGGACTAATTGATCA 17.18
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ć	1788	TGCAAATGCAGAGACACAAGCAACCTCAGCTTCCAGAAGCAGAAAGCATTGAAATCTAC 1847
0. C	1859	TGCAAATGCAGAGAGAAGAAGCIGAGCCITCTAGACCGAGAGGCATTGAAATCTAC 1918
ò	1848	CECTCTTCACTGTTTTATAAAAAGTGTATCGGCTAGCCTATCTCCGGCTAAATACACT 1907
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qq	1979	THE TOTAL OF THE TOTAL OF THE THE THE THE THE THE THE THE THE THE
ς	1968	GCACACCCTGCAGAATGAGTATGAACTCATGAGAGACAGGGATTTGGACCAAATTATGT 2027
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င်	2028	GTGTTCCATGTATGGCAAAGGAAAGAATGTAGACCTTAAATGAAATGTTGT 2087
qq	2099	GTGTTCCATGTATGGCATATGTGAAGAATATATAGACTTAAAATGCAAAATGTTGT 2158
οy	2088	AACAGCATACAAGGATCTTCCTCGTGTTGAGGAGATTGAAAACTGTGAAACTTGAAA 2147
qq	2159	AACAGCATACAAGGATCTTCCTCATGCTGTTCTTTTTTTT
Ċ	2148	AGAAGAGSASTATGATUTATTATAGTATUTATAAATOTGATCTTCATGATGAAAATGAAA 2207
QC	2219	AGAGAGGAGTATTTTTTTTTTTTTTTTTTTTTTTTTTT
δ	2208	AACAAATATTTGGAGATGCTCCACCAGGCCCCGTGTGTCACAATACCTCAAT 2267
G G	2279	AACAAATATTTGGAGTATGGTTGGAGGGGGGGTAGGTTG-CAGGAATACTCTGAGT 2337
οy	2268	TGCTCGAAGCCTTACAAGTTTCCTAGTTCACATACATTCTGGAAGAACTTA 2327
£	2338	TCCTCGAAGCCTTACAAGIIICCIAGIICACCTIACGGATTCCIGGAGGAACATCTA 2497
ογ	2328	TATTICACCCCTGAAGAGTCCATATAAAATTTCAGAAGGTCTGCCAACAACAAAAAT 2887
qo	2398	

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2.48 JACHOPAAGA FCAAGAAHOT FAGINA FORGAGA FCGGGGAOT FCGGGAGT GAGAGT S447,
                                                    2458 GACTCCAAGATCAACATAGTGATCAATGGTGAATCATCGGGGAGAAGIT 2517
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                                                                                                                                                                                                                                                                              441 H AACCATALGATACTACTACTACTACAAAAAAAATTTTCATACCTCAGAATGTTAAAAAGAACT
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protein (RTSP) of the invention. The proteins can be used for inhibiting celiciar proliferation, when coadministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RTSPs have a broader spectrum of activity than wild type RTSPs.
                                                                                                                                       Modified retinoblastoma tumout suppressor, RTSP protein; cancer therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  129 IIGGITAACTIGGGAGAAAGITICAICISIGGAIGAGIATIGGGAGGITAIATICAAAA 188
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               This sognorne engedes a modified retinoblastoma tumeur suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           93.8%; Score 3247.8; DB 19; Length 3455;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       2; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Sequence 3455 BP; 1153 A; 631 C; 627 G; 1044 T; 0 other;
                                                                                                              Modified retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      0; Mismatches
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Claim 22; Page 142 147; 249pp; English.
                                                                                                                                                        cellular proliferation inhibitor; ss.
                                                                                                                                                                                                                Location/Qualifiers
                             AAV58441 standard; DNA; 3455 BP.
                                                                                                                                                                                                                                                                                                                                                                                 (BAYU ) BAYLOR COLLEGE MEDICINE
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Matches 3352; Conservative
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                                                                                    02-DEC 1998
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                                                                                                                                                                                                                                                                                                                            19-PER-1998;
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                                                         AAV58441;
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RESULT 13
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ò :	1455 CCCATGGA	455 CCCATGGATTCTGAATGTGCTTAATTTAAAACCTTTGATTTTTACAAAGTGATCGAAAG 1514
ရှင်	1449 CCCATGGA	APPOTGAATGIGGEFFAATTTAAAAGGGTTTGATTTTTACAAAGTGATGGAAAG 1508
<i>à</i> 7	1515 TTTATO	VAAGCAGAAASCAACTEGACAAAAAAAAAGAAAAAAAAAAAAAAAAAAAAA
qq	1509 TTTTATC	NAAGCAGAAGGGAACTGACAAGAAAATGATAAAAGATTTAGAAGATGTGA 1568
ΟŸ	1575 ACATICGAA	MICATIGAATICE FIREATIGACI TITATI GALETIAA 1644
qq	1569 ACATCGA	AFCATGGAATGCGTTGCATGGCTCTCAGATTCACTTTATTTGATCTTATTAA 1628
ογ	1635 ACAATCA	AAGGACCAGAAAGGACCAACTGATCACCTTGAATCTGCTTGTCCTCTTAATCT 1694
qq	1629 ACAATCAA	AAGGACCGAGACCAACTGATTTTTTTTTTTTTTTTTTTT
ογ	1695 TCCTCTCC	ANAALAALAALAA MAGAA MALAHAHAHAHA MAGAA MAAA MAAA MAAA MAAA MAAA
qq	1689 TCCTCTCC	AGAATAATCACACTGCAGCAGATATGTATCTTTCTCCTGTATAATAATCCAAA 1748
οy	1755 GAAAAAAC	SGTTCAACTAGGGGTGTAAATTGTACTACAAATGCAGGAGACAACAAACA
qq	1749 GAAAAAA	BETTCAACTACGGGGGTGTAATTCTACGGCAAATGCAGAGAACAAACGTC 1808
ò	1815 AGCCTTCC	AGAGGGAGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
qu	1809 AGCCTTCC	SAGACCCAGAAGCATTGAAATGTAGGTTTCAGTGTTTTATAAAAAAGT 1868
ο̈́γ	1875 GTATCGGG	MARCCIAICHCASACHAAIACACH IIGTGAACCCTICTGTGTGAGCAC 1944
qq	1869 GIATCGG	TAGCCTATCTCCGGCTAAATACACTTGTGTGTTTTTTTTT
οy	1935 AGAATTAC	BARCATATCATCTGGACCCTTTTCGACGGACCTGAGGATGACTATGAATT 1994
qq	1929 AGAATTAC	SACATATCATCTGGACCCTTTCCGGCACACCCTGCAGAATGAGTGAACT 1988
ς	1995 CATGAGAC	AACAGGATTEGGACCAAATTATGATGTGTTCCATGTATGGCAAAATT 2054
q ()	1989 CATICAGAC	SACAGGCALLIGGACCAAATTALGALGTGTTCCALGTALGGAATATGCAAAGT 2048
ογ	2055 GAAGAATA	ATAGACCITAAATICAAAAICATIGTAACAGCATACAAGGATCITCTGATGC 2114
qq	2049 GAAGAATA	MAGACCTIAAATTCAAAAICATBIAACAGCATACAAGGAICTTCCTCATGC 2108
Oy	2115 TGTTCAGG	SAGAGATTCAAAGGTGTTTGATCAAAGAAGAGGGGTAFGATTCTATTATATT 2174
qq	2109 TGTTCAG	AGACATTCAAACGTGTTTGATCAAAGAAGAGGAGTATGATTGTATTATAGT 2168
ςλ	2175 ATTCIATA	AACTOGSTOTTOANGCASAGACTSAAAACAAATATTTGGASTATGGTTCCAC 2244
qu	2169 ATTCTATE	AACTEGGTETTEATGAGGGGTEGAAAGAAATALITTETAGTATTTETAA 2228
ÇŻ	2235 CAGGGCCC	SCINCETEGRONATACCICACATICCTCCACCTTACAACTITCCTAG 2294
qq	2229 CAGGCCC	CTACCTISTCACCAATACCTCACATICCTCAAACCCTTACAACTTCCTAG 2288
ΟŸ	2295 TTCACCCI	FINACGGATTCCFGGAGGGAACATCT ATATTTCACCCCTGAAGAGTCCATATAA 2354
qq	2289 TICACCO	FTAGGGATTCCTGGAGGGAACATCTATATTTCACCCTGAAGAGTCAATATAA 244B
Ś	2355 AATTFCAC	SARGULGECANTACAANTAAAAA GACCAAGA COAAGA COAGA COAAGA COAAGA COAGA
đ	2349 AATFTCAC	BAAGGTCTGCCAACAACAAAAAAAAAAAAAAAAAAAAAAA
ςλ	2415 AATTGGTC	SAATCATTCGGGACTTCTGAGAAGTTCCAGAAAAAAAAAA
qu	2409 AATTGGT	AATCATTOGGGACTTC15AGAAGT10CAGAAAIAAAIGAGGGGGGGTAIGTAA 2468
Οy	2475 CAGCCACC	CAGCGACCGTIGTIGCTICAAAAGAAGTIGCTIGAAGGAAGCAACCCTITITAAATCATTGAAAAA 2534

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27.9 166166aracigigtacanni nobalinatinatini IIIIIIIIIIIIIIIIIII 27.9 166166aracigigtaraayiii 2769
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© 15 CTUTTGTTTTTATTTATTTATATGTATATTTTTTTTTAAPTTAAPATGAACATTAGAAA 3134

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                                                                                                                                                                                                25%5 GTOCAAATTORGCAGAAACTGGCAGAAATGACTTCTACTGGAAGAGGAATGCAAAAGGA
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                                                                                                            44.55 FGTTTTTAAATGAGGATTATTGATAGT 3461
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AAV58446 Standard, DNA, 3323 BP

RESTLE 14 AAVSH446 AAV53446;

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This sequence eroodes a modified retinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   proliferation, particularly cancers. The RTSPs have a broader spectrum of activity than wild type RTSPs.
                                                                          Modified retinoblastoma tumour suppressor; RTSP protein; cancer therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        354 TATGTCAAGACTGTTGAAGAAGTATGATGTTTGTTTGCACTCTTCAGCAAATTGGAAAA; 413
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                                            Modified retinoblastoma tumour suppressor gene.
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                                                                                            cellular proliferation inhibitor; ss.
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456 654 518 714 576 774 636	834 696 894 756 954 816 1014 876	936 936 1134 996 11056 1254 1116	1314 1176 1374 1236 1434 1494 1456	1554 1416 1614 1476 1674
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1914 ACGCCTTCTGTCTGAGCACCCAGAATTAGAACATATATCATCTGGACCTTTTCCAGCACACAC
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1734 TTCTCCTGTAAGATCTCCAAAGAAAAAGSGTTCAACTACGCGTGTAAATTCTACTACTGCAAA 1744
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Medified refinedastoma tumour suppressor, RTSP protein, cameer therapy; cellular proliferation inhibitor; ss.
2814 TCITITIGEGGATATAAAATGTGCAGAGTGTTTGGGTGATTCCTAAGCCACTTGA 2873
                                                                                            2834 AATGITAGICAITGITAITITAIACAAGAITGAAAAICITGIGIAAAICCIGCCAITGAA 2933
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protein (RTSP) of the invention. The proteins can be used for inhibiting callular proliferation, when condministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular prollferation, particularly cancers. The RTSPs have a breader spectrum of
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                                                                                                                                                                                                                                                                                              This sequence encodes a modified retinoblastoma tumour suppressor
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                                                                                                                                                                                                                                               Claim 22; Page 166 170; 249pp; English.
                                                                    Xu H, Zhou Y;
(BAYU ) BAYLOR COLLEGE MEDICINE (TEXA ) UNIV TEXAS SYSTEM.
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This sequence encodes a modified retinoblastoma tumour suppressor protein (RISP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a pf3 protein. The prsps can be used for treating diseases characterised by abnormal cellular.
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[7] PhoPasaLeuLysdlulleAspThrSerThrLysValAspAsaAlaMetSerArgleu 120
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1 MetProProLysThrProArgLysThrAlaAlaThrAlaAlaAlaAlaAlaAlaGluPro 20
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         cell cycle can be receibly arrested in a cancenient and safe amount. The protein is used in a compan is relatively inexpensive and readily obtainable, and shows little or no toxic effects on healthy cells. It is also compatible with other methods and devices
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   for regulating certain physiological processes of the hody, such as blood cell produ, and gamete produ. Fragments of the protein are solable in low concist of alycerol thus enhancing their value in
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                The sequence is that of the retinoblastoma gene which encodes the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Method of controlling cell cycle progression \cdot uses purified retinoblastoma protein or fragment, for use in combination with
                                                                                                                                                                                      RB gene product; p56RB portion; cell cycle progression control;
                                                                                                                                                                                                          combination; therapeutic methods; arrest; tumouriquaesis; requiation; physiological processes; blood cell produc
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Sequence 2994 HP; 974 A; 618 C; 594 C; 808 1; 0 other;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Goodrich DW, Lee EYHP, Lee WH, Wang NP;
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                                                                                                                                                                                                                                                                                                                                                            /*tag= a
/note= "Rb protein"
                                                                                                                                                                                                                                                                                                                         Location/Qualitiers
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                                   AAQ41545 standard; DNA; 2994 BP.
                                                                                                                                                                                                                                                                                   Homo sapiens SR-40 cell line
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   910S-0778510.
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                                                                                                                                                  Retinoblastoma gene.
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                                                                         AAQ41545;
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يد	1.4.1	TELLETETETETETETETETETETETETETETETETETE	258
<u>></u> 4	41	AspteutroteuValarqteuGlutheGluGluthrGluGluthroAsptheThrAlateu siliiilililililililililililis saccigotictestroksecttqacittqacittiqaAsaAcAsqAsqAccactGATTTACTGCATTA	60 318
. <u>Ş</u> ~	7	CysciniysLeulyslleProAspHisValArgCluArgAlaTrpleu	76
. 	113	TGTCAGAAATTAAAGATACCAGATCATCAGAGAGAGAGCTTGGTTAACTTGGGAGAAA	378
<u>~</u>	76		92
4	4.7.4	-3111CAL/10TGGATGGAGTATFGGGAGGTTATATFFGAAAAGAAAAAAAA	438
<u> </u>	4.49		89 498
<u> </u>	7	SINLYSASDITEGTUTESETVATHISTYSPEEPREASDEGTEGTYSGTUTEASPTHT STITTHTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	109
· .	110	SerThrLysValAspAsnAlaMet SerArdLeuLeuLysLysTyrAspValLeuPheAla	129
۾	488	#	618
<u>ئ</u> د ~ي		LeupheserLysLeuGluArqThrCysGluLeuIleTyrLeuThrGlnProSerSerSer 	149
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بند	6.29	* 1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.	738
<u>ن</u> . ج		AlaLysGlyGluValLeuGlnMetGluAspAspLeuVallleSerPheGlnLeuWetLeu 	189 798
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<u>ب</u> ج	(E)2 (E)4	HisslurysAsnlleAspGluValLysAsnValTyrPheLysAsnPhelleProPheMet 	269
. <u>.</u>)	AsnSericoudlyLeuVallhrSerAsnGlyLeuProGluValGluAsnLeuSeriysArg	289 1048
, ₂₀ <u>2</u>	E 5	TyroluolulleTyrLeuLysAsnLysAspLeuAspAlaArgLeuPheLeuAspHisAspleidannannannannannannannannannannannannann	309 1158
> 4	410	4	329
:~ <u>a</u>	45	ASILEUASPELUCTUVATASNVATTIEPTOPTOHTSTHEPTOVATAEGIHTVATMETASN 1-1-11-11-11-11-11-11-11-11-11-11-11-11	349 1278

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2239 GAYYAAATTATGATGTECTECATGTATGEGATATGCAAAGTGAAGATATAGACTTAAA 2298
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                                                                                                                                                                                                                                     2059 CCATTGAAATCTACCTCTCTTTCACTGTTTTATAAAAAGTGTATCGGCTAGCCTATCTC 2118
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                                                                                                                                                                              410 IleGlySerGlnArgTyrLysLeuGlyValArgLeuTyrTyrArgValMetGluSerMet 429
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                                                        470 HeSerTyrbbeAssAssoysthrValAssprotysGlaSettlettettysAtaValitys
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2419 ATGCAGAGACTGAAAACAAATATTTTGCAGTACCACGCCCCTACCTTGTCA 2478
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                                                                                                                                                                                                    750 ProlleProHislleProArqSerProTyrLysPheProSerSerProLeuArqIlePro 769
                                                                                                                                               778 GlyGlyAsmlleTyrIleSerProLeuLysSerProTyrLysIleSerGluGlyLeuPro 789
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                                                                                                                                                                                                                                                                                                                8.00 ArqSerAladluGlySerAsnProProLysProLeuLysLeuArqPheAspIleGlu 849
                                      7.00 MetelluArglandystlarAsutleleuGlufyrAlaSerThrArgProProflarLeuSer 749
                                                                                                                                                                                                                                                                                                                                                                     850 GtySerAspdtuAlaAspdtySerLysHisLenProClyGtuSerLysPheGlnGlnLys 869
                                                                                                                                                                                                                                                                                                                                                                                                                         870 LeuAlaGluMetThrSerThrArgThrArgMetGluLySGluLySMetAsnAspSerMet, 889
bladder cancer; restenosis; angioplasty; diabetic retinopathy, thyroid hyperplasis; charc's disease; psoriasis; benyani prostatic hypertrophy; Li Frammen, syndrome; peripheral vascular disease; therapy, ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Retinoblastoma profein RB; E2E, transcription factor, human
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Location/Qualifiers
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Antelman D. Gregory RJ, Wills KN;

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4.49 ATCTGTATCTTATTGCAGGACTAGATGAGATGAGATGTCATTTTATTGAGTA 4.98
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       41 AspLeuProLeuValArgLeuGluPheGluGluGluThrGluGluProAspPheThrAlaLeu 60
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  transcription of the E2F promoter than Rb alone and cause cell eyele
                                                                                                                                                                                                                                                                                                                                                                                                                                            iscase. Tissue specific expression of EZF-RH instants is The fusion proteins are more effective in repressing
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                                                                                                                                                                                                                                                                                                                                                                                                                       benign prostatie hypertrophy. Li Fraumeni syndrome and peripheral
                                                                              New tusion polypeptide of, e.g. transcription factor use treat, e.g. hyper-proliferative disease such as cancer and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Sequence 2994 BP; 974 A; 618 C; 593 C; 809 1; 0 offer;
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                                                                                                                                                             Example 1; Fig 2A; 91pp; English.
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full length, wild type RR (wtkH) cDNA probe to a coll sample and detecting a mutated KH furleic acid. The method is useful as a diagnostic tool for diagnosing retinoblasiona. RB cDNA or genomic DNA are preferably
                                                                                                                                                                                                                                                                                                                                                                           MA gene; human; retinoblastama gene; mutation detection; immunoscreening; retinoblastoma disquosis; hereditary retinoblastoma; secondary cancer; cattesatroma; libroaricma; dibolastoma; breast cancer; tumouriquensis suppression; sa.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           used as probes to determine the defect region of the MRB gene through genomic DNA blotting analysis of using the method of restriction fragment
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   length polymorphism analysis to determine the diseased allele. Cloned PB
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  This sequence represents the wild type human retinoblastoma gene. The invention relates to a method of detecting a mulated retinoblastoma (mRB) nucleic acid in mammals comprising hybridizing an isolated
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              cancer, such as, ostrosarcoma, fibrosarcoma, glioblastoma, breast cancer whether or not conterted with retinoblastoma. The method is also used in the suppression of tumouriqueesis where the absent RB protein pages13 will be provided through the molecular industion and genetransplanting of the Rb cDNA to the individual in need of ppRB110.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                diagnostic method is particularly intended for use in screening
ramilies with a history of hereditary retinoblastoma and for screening
                        cDNA can be used to generate specific anti-RB protein (anti-ppRB110) antibodies which are useful for Immunosereening of tissue biopsy. The
870 Lonaladlumerthrsorthrandlhrangmerdinlysglulysmeraspassermer 889
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             4.0 LysThrLewMnThrAspSerIleAspSerPheGluThrGluArqThrProArqLysSer 329
                                                                                                                                                            330 AsnicuAspCluGluValAsnVallleProProHisThrProValArqThrValMetAsn 349
                                                                                                                                                                                                                                                                                                                        Fig. thriteGinGinLenMetMetHeLeuAsnSerAlaSerAspGinProSerGluAsnLcu 369
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     170 IleserTyrPhcAsnAsnCysThrValAsnProLysGluSerIleLeuLysArqValLys 389
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     390 AspiledlyTyrilePhelysClutysPheAlaLysAlaValClyClnClyCysValGlu 409
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2659 ACTICIGAGAGATICCAGAAAATAAATGAGAGGAGGATGAACGAAGGAGAGGAGAAA 2716
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 830 ArqSerAlaGluGlySerAsnProProLySProLeuLySLysLeuArqPheAspIleGlu 849
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       850 GlySerAspGluAlaAspGlySerLysHisLeuFroGlyGluSerLysPheGluCluLys 869
                                                                                   690 PhelysllelleValThrAlaTyrLysAspleuProHisAlaValGluThrPhelys 709
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         870 LouAlaGluMetThrSerThrArgThrArgMetGlnLysGlnLysMetAsnAspSerMet 889
                                                                                                                                                                                                                                                                                                                                                                                                                                                                            2239 GACCAAATTATGATGTTCCATGTATGTATAIGCAAAGIGAAAGATAATAAACCTIAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          770 GlyglyAsmileTyrileSerProLeuLysSerProTyriysIleSerGludlyLeuPro
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                                                                                                                                                                                                                                                                                                                        730 MetalnArqLeuLysThrAsnIleLeuGlnTyrAlaSerThrArqProProThrLeuSer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               810 ThrSerCinTySPheGiniysTleAsnCinMetValCysAsnSerAspArgValLxculys
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cell cycle; p53; mitosin; cell death; apoptosis; thymidine kinase;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Human; pl10-RB; retinoblastoma; tumour suppressor; gene therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Human pll0-RB retinoblastoma tumour suppressor encoding cDNA.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      "retinoblastoma tumour suppressor"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Location/Qualifiers
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Tue Jan 21 10:03:49 2003

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The present investion describes a composition comprising a recombinant addenovirus expression vector, where the vector has an insert of exceptions DNA comprising a gene encoding a loreign protein and adenovirus DNA in which all of the coding sequences of Ela, Elb, and protein IX, and part of Es are deleted. The vectors are useful in gene thorage treatment of cancer, especially for treating ps3 deficient unious. The vector enables saler and more ellicient quee therapy of cancer. The present sequence encodes human pilo-RB relinoblasional unious suppressor which can be used as the foreign quee in the above
                                                                                                                                                                                                                                             Percombinant adenoziral vertors useful for gene therapy of cancer, especially p53 delicient tumours
                                                                                                                                                                hequiy RJ, Maneval DC, Wills KN;
                                                                                                                                                                                                                                                                                          baselosure; Fig 3, 50pp; English.
                                           940S 0142669.
940S 0142669.
940S 0246006.
970S 0959648.
               9705 0959638.
                                                                                                                                                                                              WP1: 1999 44358/47.
                                                                                                                               (.'AN.I ) ('AN.II INC'
                                                                                                                                                                                                               P. PSDB; AAY24471.
             28 CH 11997;
                                             25 Oct 1994;
25 Oct 1993;
                                                                           19 MAY 1994;
28 OCT 1997;
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Sequence 2995 BP; 975 A; 618 C; 593 G; 809 L; 0 other;

1639 ACTACATCTCACAACTTCATTCTCCAAACATTTCTCTTTCCCATCCATCTCTCAATGTC 1698

q

Q()	559	AGTACCAAAGTTGATAATGCTATGTCAAGACTGTTGAAGAAGTATGATGTTTGTT	6 18
ć	130	LeuPheSerLysLeuGluArqThrCysGluLeuIleTyrLeuThrGluProSerSerSer	149
qq	619	CTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATATTTGACAYAACCAGGAGTTCG	4.78
οy	150	HesorThreInHeasiseralaLouValloulysvalsorTrpHethreboulou	59
qq	629	ATATCTACTGAAATAAATTCTGCATTGGTGCTAAAAGTTTCTTGGATCACATTTTTTA	7.48
Ś	170	AlaLysGlyGluValLenglnMetGluAspAspLenVallleSerPheGlnLenMetLen	18%
qq	739	GCTAAAGGGGAAGTATTACAAATGGAAGATGATCTGGTGTTTCATTTCAGTTAATGATA	3.68
Ś	190	CysValLeuAspTyrPhelleLysLeuserProProMetLeuLeuLeutyeslabroTyrLys	507
op	799	TGTGTCGTTGACTTTTATTAAACTCTCACCTCCCATGTTGCTCAAAGAACCATATAAAA	8. 3.
ν̈́ο	210	ThratavaliteprolleAsnGlySerProArgiba ProArgArgetygibashArger	5
43	858	ACAGCIETATACCCATTAATGGTTCACCLCGAA ACCAGGGGAGGTCAGAAA AGGAGT	918
ςŏ	230	AlaArqIleAlaLysGlnLeuGluAsnAspThrArqIleIleGluValLeuf, stysGlu	249
qo	919	GCACGGATACCAAAACAACTAGAAATGATACAAGAATTATTGAAGTTCTCTGTAAAGAA	478
οχ	250	HisGluCysAsnIleAspGluValLysAsnValTyrPheLysAsnPheTleProPheMet	697
q	979	CATGAATGTAATATAGATGAGGGGGGAAAAATGTTTATTTCAAAAAATTTTATTTTTTTT	1038
οy	270	AsnSert.cuGlyl.cuValThrSerAsnGlyl.cuProGluValGluAsnIcuSerTlysArq	289
qq	1039	AAITCICITGGACITGIAACAICTAAIGGACITGCAGAGGITGAAAATCI TCIAAAAGGA	1098
5	290	TyristastuttetyrisestysAsnikysAspieuAspAtaArqleufheteuAspilisAsp	404
qu	1099	TACGAAGAATTTATCTTAAAAATAAAGATCTAGATGCAAGATTATTTTTTTT	1158
QY	310	LysThrLeuGlnThrAspSerIleAspSerPheGluThrGlnArqThrProArqLysSer	456
qq	1159	AAAACTGTTGATGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTT	1218
Οy	330	Asn.ceuAspGluGluValAsnVallTeProProProHisThrProValArqThrValMetAsn	344
qq	1219	AACCTIGATGAAGAGGTGAATGTAATTCCTCCACACACACTAATTATTATGAAA	1278
λο	350	The ilectric later Met IleLeuAsassetAlaserAspointroserol aAsaLeu	£9\$
qn .	1279	ACTATICCAACATTAATGATGATTTTAAATTCAGCAAGTGATCAACTTTTAGAAAATCTG	1338
ογ	370	IleSerTyrPheAsnAsnCysThrValAsnProLysGluSerIleLeuLysArqValLys	484
qa.	1339	ATTICCIATITIAACAACIGCACAGIGAATCCAAAAGAAAGITATACIGAAAAGAGIGAAG	1398
. OY	340	ASP11eG1yTyT11ePhetysC1u1ysPbeAlatysAlaVa1G1yC1nC1yCysVa1G1u	404
Ωp	1399	GATATAGGATACATCITITAAAGAGAAATITGCTAAAGCIGIGGGAAAAGTTGTCGAA	1458
Qy	410	lleGlySerGlnArqTyrLysLeuGlyValArqLeuTyrTyrArqValMetGluSerMet	424
qn	1459	ATTGGATCACAGCATACAAACTTGGAGTTCGTATTACCGAGTAATGGAATCATG	1518
Οŷ	430	LeuLysSerGluGluGluArqLeuSerIleGluAsnPheSerLysLeuLauAsnAspAsn	443
qq	1519	CTTAAATCAGAAGAAGAAGATTATTATTATTATTATATTATTATTATT	1578
ОУ	450	TePbeHisMetSert.coulcoullaGysAlalcuGluValValMetAlaThr19rSerArg	469
qq	1579	ATTITCATATGTCTTTAITGGCGTGCGCTCTTGAGGTGTAATGGCCACATATAGCAGA	16.48
ò	470	SerThrSerGlaAsaLeuAspSerGlyThrAspLeuSerPheProTrp11eLeuAsaVal	48.5
á	1630	A COLOR OF A COLOR OF	16.00

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1699 CITAATITAAAAGCCTITGAFITTTACAAAGTGATCGAAAGTTTTATCAAAGCAGAAGGC 1758
                                                                                                                                                                                                    1819 311GCA1GGCTC1CAGATTCACCTT1ATTTGATCTTATTAAACAATCAAAGGAGCGAGAA 1878
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                                                                                                                                                           540 LeuAlaTrpLeuSerAspSerProLeuPheAspLeuIleLysGlnSerLysAspArgGlu 549
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4 on LenAsnicontysAlaPheAspPheTyrLysVall1eGIuSerPhelletysAlaGluGIy 509
                                                                                                                                                                                                                                                                                                                                                                                                      *** AraValAsuSerThrAlaAsnAlaGluThrGlnAlaThrSerAlaPheGlnThrGlnLys 609
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   650 TrpThrLeuPhedlnHisThrLeudlnAsnGluTyrGluLeuMetArqAspArqHisLeu 669
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               for the LystletleValThrAlaTyrLysAspleuProHisAlaValGlnGluThrPhelys 709
                                                                                                The AsideathrAngthaMetileTysHisterGluAngCysClaHisAnglLeMetGluSer
                                                                                                                                                                                                                                          55-0.3:yProff:AspHistenGluSorAlaCysProLeuAsnLeuProLeuGlnAsnAsnHis
                                                                                                                                                                                                                                                                                                                         570 ThrAlaAlaAspMetTyrLeuSerProValArgSorProLystystysGlySerThrThr
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The present invention describes an adenovital expression vector comprising a deletion in the protein IX gene and a gene encoding a fereign protein. This vector can be used in 3em therapy, particularly to introduce tumour suppressor genes into neuronous cells, Genes which may be used include p53, thymidine kinese and retinoblastoma tumour suppressor gene (Rb). The present sequence is the retinoblastoma tumour
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Recombinant adenovirus expression vector comprising a partial or total deletion of a protein IX DNA and a gene encoding a foreign protein e.g. suicide protein, useful for inhibiting or reducing the proliferation of
                           2779 GGATCAGAIGAAGCAGAIGGAAGTAAACAICICCCAGGAGAGICCAAAITTCAGCAGAAA 2838
850 ClySerAspCluAlaAspClySerLysHisLeuPreClyCluSerLysPheCluClnLys 869
                                                        Retinoblastoma; tumour suppressor protein; Rb; p53; cancer; adenoviral vector; gene therapy; thymidine kinase; ds.
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                                                                                                                                                                                                                                                                                                         Retinoblastoma tumour suppressor gene.
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                                                                                                                                                                                                                 AAH25755 standard; DNA; 2995
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96.66%
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Retinoblastoma, RB: tumour suppressor protein; pl10RB; p53; gene therapy; cytistatic actifityroid: antipsoriatic, adenoviral protein IX, psuriasis, throid hyperplasia, Grave's disease, hepatocullular carcinoma, neoplasm, because prostatic hypertrophy; Li Francomen syndrome; sickle cell anamia; Fi, stelle dietro; legammia, lymphoma; adenoviral carcon; ss.
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p110RB"
                                                                                                                                                                                                                                                                                                                                                         Retinoblasiona tumour suppressor protein, pl10RB cDNA.
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protein, designated as p1088.

The twention relats to recombine the cities expression solution that stars to recombine the control of the adenoviral protein IX ENA beginning at molecides 357 or 369 and ending at 4030-4050, and having a gene encoding a foreign protein such as tumour suppressor protein. Such protein protein such as tumour suppressor for screening tumour suppressor as a sed for screening tumour suppressor agence useful in gene therapy. The vector is particularly ascful for treating or reducing hyperproliferative cell disorders such as thyroid hyperplasia. Grave's disease, psoriasis, tender the hypertrophy. It is also the second in suppressor as thyroid hyperplasia. Spathome, autoris specifically heppalocellular carcinoma, neoplasms, leukaemias, lymphomas, etc. to inhibit tumour proliferation or to medicine particular related by the second for the second and any sease.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                New recombinant ademovirus expression vector having a gene encoding for a foreign protein and a partial or total deletion of the ademoviral protein IX DNA, useful in gene therapy for treating or reducing hyperproliferative cells.
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Oy	5 3 0	LeuAlaTrpLeuSerAspSerProLeuPheAspLeuTleLysGInSerTysAspArgülu 549
<u>q</u>	1819	CTTGCATGGCTCTCACATTCACCTTTATTTATTTATTTAT
Ś	550	61yProThrAspHisLeuGluSerAlaCysProLeuAsnLeuProLeuGlnAsnAsnHis 569
qc	1879	GGAGCAACTGATCACCTTGAATCTGCTTGTTAATCTTCTTCTTCTAGAATAATCACTT938
oy.	570	ThrataalaaspMet lyrteuScrProValArdSerProtystlystlystlythrib 146 589
g G	1939	ACTGCAGCAGATATGTATCTTTCTCCTGTAAGATCTCCAAAGAAAAAAGGTTCAACTACG 1998
ο _γ	290	ArqvalAsnSerThrAlaAsnAlaGluThrGlnAlathrSerAlaPheGlnThrGlnLys 609
qq	666	CCFCTAAATICTACIGCAAAIGCAGAGAGAGAAACCAAAAIGAGAATITAGAGAAAAAAAAAA
Ś	610	ProLeuLysSerThrSerLeuSerLeuPhoTyrLysLysValTyrArqLeuMaTyrLeu 629
<u>a</u>	2059	CCATIGAAATCTACCICICITICACIGITITATAAAAATIGTATCGGTAGCTALCIC ZIIB
οy	6 40	Argleudsmithileutyschaargleuteuserchan) sprochalendinhisiteite 649
qq	2119	COSCIDADATACACTITGIGAACGCTTCTGTCTGAGCACCCAGAATIAGAACAIAICAI 2178
ΟŸ	650	Trp1hrLeuPheGlnHisThrLeuGlnAsndlutyrGluLeuMetArgAspArgHisLeu 669
QC	2179	FGGACCCT FTTCCAGCACACCTGCAGAA LGAGTATGAACTCATGAGAGACAGATTG 2238
ς	670	AspointleMetMetCysSerMetTyrGlyHeCysLysValLysAsnileAspleadys 689
qq	2239	GACCAAATTATGATGTTGCATGTATGCATATGCAAAGTGAAGAATTATAGACTTTAAA 2298
Οy	069	PhetysiletteValThrAlaTyrtysAspteuProHisAlaValdinGtuthrPhetys 709
Db	2299	TTCAAAATCATTGTAACAGCATACAAGGATCTTCCTCATGCTGTTCAGGAGACATTCAAA 2358
ΟŸ	710	ArqvalLculletysGluGluGluGluGluTyrAspSerTletTeValPheTyrAsnSerValPhe 729
ď	2459	CCRGPTTTTCATCAAAGAAGAGAGTATCATTCATTATTCTTTTTAACCCGCTCTTTTTTTT
ς	7.50	MetGloarqleuLysThrasolleLeuGloTyralaserThrargroProThrLeuser 749
qc	2419	ATGCAGAGACTGAAAACAAATATTTTGCAGTATGCTTCCAGGAGGCCCCTAPCTTGTCA 2478
οy	750	ProffeprodistreprodigserProtyrLysPheboserSerProtendrqffePro 769
qq	2479	CCAATACCTCACATTCCTCGAAGCCTTACAAGTTTCCTAGTTCACCTTACGATTCCT 25.88
ΟŸ	770	61y61yAsn11eTyr11eSerProteutysSerProTyrtys11eSerG1a61y1caPro 789
qn	2539	GGAGGGAACATCTATTTTTTTTTTTTTTTTTTTTTTTTT
ολ	750	ThrProThrLysMetThrProArgSerArg11eLeuValser11e61y61uSerPhe61y 809
qc	2599	ACACCAACAAAATGACTGCAAGATCAAGATCTTAGTATTGTTGTTGTTGTTGTTGTT
Oy	810	ThrSerGlutysPhectnLysTleAsnCluMetValCysAsnSerAspArdValLeutys #29
qq	2659	ACTTCTGAGAAGTTCCCAGAAAATAAATCAGATGGTAACAAAAGAGGGGGGGG
ολ	8 30	ArgSerAlaGluGlySerAssProProLysProLeutyslysLeuArqPleAsp11e31n 849 HIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII

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Who mitnein coll death adenoviral protein IX, quae thorapy, cylosiatic, a benevirus expression vector, tumour, non-small cell lung cancer, small cell lung cancer, hepatocarcinoma, hepatocellular carcinoma, melanoma; retinoblastoma; colorectal carcinoma; sarcuma, Wilm's tumour, astuckytoma, alioblastoma, neuroblastoma; ovarian carcinoma; content cancer, qene, ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     can have eytostatic activity and be used in gone therapy. The recombinant advanceins expression vector is particularly useful for treating or suppressing proliferation of a tumour, e.g. non-small cell bing cancer, small cell lind cancer, small cell lind cancer,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               The present invention describes a recombinant adenovirus expression vector, which omprises a partial of related of a protein {\bf X} EMA and a gene encoding a foreign protein. The recombinant adenovirus vector
                                                                 melanoma, retinoblastoma, breast tumour, colorectal carcinoma, sarcoma,
2/19 AGANGEGEGAAGGAAGCAAGCEEEAAACCACEGAAAAAAAACEAGGCEFFGATAFFGAA 2778
                                                                                                                                                                                                                                                                         87. LeuAlaGluMetThrSerThrArgThrArgMetGluLysGluLysMetAsuAspSctMet 889
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    "retinoblastoma tumour suppressor protein"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Retinoblastoma: tumour suppressor protein, pil0 RB, cell cycle: p53;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  New recombinant adomewinal vector comprising a partial or total deletion of a protein IX DNA and a gene encoding a foreign protein, useful in gene therapy, particularly for treating or suppressing
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Refleoblastoma tumeur suppressor pretein pl10 RB encoding cDNA.
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prostate tumour, bladder tumour of the reticuloendotheliai
lissues, Wilm 's tumour, astrocytoma, dliohlastoma, neuroblastoma, oversionae,
overian carcinolus, ostrocarcoma of renal cancer. The present sequence
encodes the retinoblastoma tumour suppressor protein pli0-kH, which is
                                                                                                                                                                                                                                                                                                                                                                                                                                                         279 GITH'AHHERGATGGAGTATTGGGAGGTTAINTTCAAAGAAAAAGAACTGTGGGGA 438
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                                                                                                                                           Sequence 2335 BF, 375 A, 618 C, 593 G, 809 T; 0 Other;
                                                                                            given in the exemplification of the present invention.
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Mismalches:
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Modified retinoblastoma tumour suppressor; RTSP protein; cancer therapy;
2239 GACCAAATTATGATGTGTTCCATGTATGCATATGCAAAGTGAAGAATATAGACCTTAAA 2298
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                                                                                                                                                                                    670 AspClb11cMctMctCysScrMctTyrCly11cCystysVallysAsb12 AspLcB1ys 689
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cellular proliferation inhibitor; ss.

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This sequence encodes a modified relimoblastoma tumour suppressor profein (RISP) of the invention. The profeins can be used for inhibiting contains proffication, when cradministered with a pSA profein. The PISPs can be used for treating diseases characterised by abnormal cellular profiferation, particularly cancers. The RISPs have a broader spectum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         ATCTGIATCTITATTGCAGCAGTAGACCTAGATGAGAGATGTCGTTCACTTTACTGAGGCTA 366
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proteins which can be used for treating diseases characterised
                   2587 AGAACTICCTICAACCAACCCTICCTAAACCACAAAAAACTAACCTTTTGATATTIGAA 2646
                                                                                           2647 GGATCAGATGAAGGAGATGGAAGTAAAGATCTCCCAGGAGAGTCCCAAATTTCACCAGAA 2706
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                                                                                                                              870 LeuAlaGluMetThrSerThrArgThrArgMetGlnLysGlnLysMetAsnAspSerMet 889
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    The present sequence appears in the specification, which describes a fetracycline responsive expression vector (iRPV), which contains a sequence encoding a fusion protein comprising a transcriptional transactivation domain (TTD) operatively attached to a fetracycline
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     tetracycline operator. The TREVs can be used to produce stable cell
lines in which gene expression is tightly requiated by tetracycline.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            repressor protein (164), the first sequence operatively positioned downstream of a promoter. The vector also contains a cloning site operatively positioned demostream of a basal promoter comprising a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Minimal promoter, tetracycline responsive expression vector, TREV, transcriptional transactivation domain; TTD; tetracycline repressor protein; TRP; tetracycline operator;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         New tetracycline responsive expression vectors—used for the tightly controlled expression of genes, such as tomour suppressor genes for treating cancers
they can be used for the production of proteins such as tumour
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         production, stable cell line; protein production, tumour suppressor protein; treatment; cancer; ss.
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Sequence 3555 BP; 1171 A; 684 C; 653 G; 1047 1; 0 other;

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5 8	11:1	SerThrLysValA 	SPASDAJAMEUSEFAI 	rqLeuLeuLysLysTy 	graspValLeuPheAla 	129
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5 E	170	AlaLyssiyGluV 	albeuglnMetgluAs 	spAspLeuVallleSe 	erPheGlnLeuMetLeu 	189 666
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5 E	2 + 2 F#7	AlaAraileAlaL 	yodloLeudluAcoAc 	opikrargileiled 	luValLeuCysLysGlu 	249 846
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               490 Leudsmileutzsalarhedsprietzriysvalflechuserrheiletysalachucty
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hEST2; telomerase; catalytic subunit; reverse transcriptase; life-span; rethroblastema; p53; tumour suppressor; inhibitor; arteriosclerosis; proliferation; numortal; tumour therapy; macular degeneration; activator;
              2467 ACACCAACAAAATGACTCCAAGATGAAGATCTTAGTATGAATTGGTGAATGATTGGGG 2526
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                                                           670 AspellniloMetCysserMetTyrGlyileCystysVallysAsmiloAspieutys 699
                                                                                                                     690 PhetystletleVallhrAlatyrt.ysAspteuProHisAlaValGlnGlufhrPhetys 709
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Homo sapiens.
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treat conditions related to (premature) agains, e.g. macular degeneration and arteriosclerosis. The cells can also be used to replace tumour cell
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              lines in vitro and for studies on biochemical and physiological aspects of growth and differentiation. Long lived (immortal) cells could also be of use in the production of normal or genetically engineered
                                                                                                                                                                                                                                                                                                                                                                                                                 The invention concerns methods and reagents for extending the life span,
                                                                                                                                                                                                                                                    New method for increasing the prollierative capacity of cell lines comprises administering agents reversibly activating felomerase activity and reservely increases activity and reserve the increases in treating age related discases
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               what drouprotein which bypasses K and/or p3. Antisease constructs of the Rb and pl61NK4a genes may also be used. The methods are useful for increasing the proliferative capacity of eeits, the cells are
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    increasing the proliferative capacity of eeils, the cells are subsequently of use in pharmaceutical and cosmette preparations used to
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                                             98US-0109891.
                                                                      99US-0120549.
99WO-US27907
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                                                                                                                 (GENE-) GENETICA INC.
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24 - NOV - 1999;
                                             25-NOV-1998;
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The present sequence encodes a human androgen receptor coactivator designated Kb. Androgen receptor co-activator proteins from the present havinton can be used in servening assays to identify candidate pharmacentical molecules for the ability to promote or inhibit the interaction of androgen receptors and androgen responsive elements to modulate androgenic activity. The identification and characterisation
                                                                                                                                                                                                                                                                                             28.88 CPGOCAGANANATGACTTCTACTCGANCACGAAATGCAAAAGCAGAAAATGAATGATGCAAGA
                  271B AGAAGTGGTGGAAGGAAGCAAGCTGGTAAAGCAGAAAAAGTACGTTTGATATTGAA 2777
                                                                                                                                                                                                                                          2778 GGATGAGAAGGAGAGGAGTIGGAAGTAAAGATGTGGGAGGAGGAGAGTTTGAGGAGAA 2837
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Novel androqem receptor associated proteins used to detect androgemic or antiandroqemic activity in screening assays for candidate pharmaceutical molecules which promote or inhibit the activity.
790 FhrProThrLysMetThrProArdSerArdIleLeuValSerileGlyGluSerPheGly 809
                                                                                                                                      839 ArdSerAlaGluGlySerAsnProProLysProLeulysLysLeuArgPheAsp11eGlu 849
                                                                                                                                                                                                         850 ClyserAspeluAlaAspelySerlysHisLearnoSycluserLyaFbeslnGldlys 869
                                                                                                                                                                                                                                                                               870 LouAlaGluMetThrSerThrArgThrArgMetGlnLysGlnLysMetAsnAspSerMet 889
                                                                  810 thrserGlutysPheGlutysTleAsnGlnMetValCysAsnSerAspArgValLeutys 829
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Human; androgen receptor coactivator; ARA54; ARA55; ARA24; detection;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   antiandrogenic; identification; prostate cancer; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Human androgen receptor coactivator Rb encoding conA SEQ 1D NO:7.
                                                                                                                                                       /note- "androgen receptor coactivator"
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2898 GATACCECAAGGAAGAAA 2921
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of androgen receptor co-activators such as those of the invention will facilitate the development of screening assays to evaluate the potential
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                                     efficacy of drugs in the treatment of prostate cancer.
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nman; cancer; colon; breast; ovary, ossophagus, kidney; thyroid;
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dostatic; gene therapy; antineoplastic; Wilm's tumour; adenocarcinoma;
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(AVAL.) AVALON PHARM.

Endress G, Horrigan S; Carter KC, Ebner R, Auqustus M, Weaver Z: Sopport DR, Young PE,

WPI: 2002 188264/24.

chemical agent to be rested for anti-neoplastic activity, and determining a change in expression of a gene of a signature gene set Screening for anti neoplastic agent involves exposing cells to a

claim 1; SEQ ID 1210; 44pp; English.

The present invention describes a method (M1) for screening for an anti-neoplastic agent. The method involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, determining a change in expression of at least one gene (I) of a signature gene set, where (I) comprises a sequence (S) selected from 8447 sequences (given in ABL61664 to ARL70110), or is at least 95% identical to (S), where a change in expression is indicative of anti-neoplastic activity. (I) has eviostatic artitity and can be used in gene therapy. MI can be used for screening an anti-neoplastic agent, and can be used for producing a product which

210 ThralaValileProlleAsnGlySerProArgThrProArgArgClyCluAsnArgSer 229

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is the data collected with respect to the anti-neoplastic agent as a result of ML, and the data is sufficient to convey the elemical structure and/or properties of the agent. M. can be used in the treatment of cancer such as colon, breast, stomach, lune, thytoid, oesophageal, ovarian, kidney, prostate or pancreatic cancer, adenocarchnoma, carcinoma, clear cell cancer, infiltrating ductal cancer.
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Recombinant; adenovirus; expression vector; TSG; small lung cancer; tepatocarcinoma; melanoma; retinoblastoma; sarcoma, sickle cell, anaemia; tay-Sach's disease; ss.

Home saprens

Location/Qualitiers 149. . . 49.5 Κ•••

/*tag= a

W09511984 A.

04 MAY 1995.

94WO-US12235. 12 OCT 1994;

94US 0246007. 930S:0142669. 19 MAY 1994; 25 OCT 1994;

(CANJ) CANJI INC.

Wills KN; Gregory Rd, Maneyal DC,

WPI; 1995 178876/23. P PSDB; AAR74271.

foreign gene csp. encoding tumour suppressor protein for gene therapy of tumours, reduces contamination by wild type adenovirus Adenoviral vector with deletion of viral protein IX contains

Dischosure; Fig 3; 92pp; English.

tumour protein. The gene can be used in a movel method involving a recombinant adenovirus expression vector to treat diseases associated with the ansence of the TSG or the presence of a mutated TSG, e.g. many forms of carcinoma, sickle cell anaemia or Tay Sach's the sequence is that of the DNA sequence encoding a retinoblastoma disease.

Sequence 2995 HP; 975 A; 617 C; 594 G; 809 T; 0 other;

Sec also AAU90060-5.

968 Conservative: Mismatches: Matches: Indels: in third 4601.50 96,55**%** 99,46**%** 899.96 Best Local Similarity: Percent Similarity: Aliqument Scores: Query Match: DB:

18 09 026 459A 41 (1 897) x AAU96059 (1 2995)

21 ProAlaProProProProProProProGluGluAspProGluGlnAspSerGlyProGlu 40 41 AsptæuProfæuValArdfænGluPheGluGluThrGluGluProAspPheThrAlafæu 60 1 MethroProLysThrProArgLysThrAlaAlaAlaAlaAlaAlaAlaAlaAlaAlaAlaAlaGluPro 20 61 CyschntysteutystteProAspHisValArdGluArgAlaTrpleut ŝ 5 5 Ξ 5 ÷ $\stackrel{>}{>}$ = 5

79 GILLMAICTGTGGALGGAGLALFGGGAGGTLAFAITGAAAAGAAAAAGAAAGGAAGTGTGGGGA 438

-ValAspLeuAspGluMetSerPheThrPheThrGluLeu 89

1218 979 CATGAATGTAATATAGATGAGGTGAAAAATGTTTATTTCAAAAATTTTATATATTTTATG 1038 279 ACTATICCAACAATTAATGATGTTTTAAATTAAGGAAGTGATGAAAAATTGAGAAAATTTAA 399 GATATAGGATACAICITIAAAGAGAAATIIGGITAAAGAGAGGTIGIGIGGAGA 1458 390 AsplleClyTyrllePheLysCluLysPheAlaLysAlaValGlyGlnClyCysValGlu 409 410 IleGlySerGlnArqTyrLysLeuGlyValArqLeuTyrTyrArqValMetGluserMet 429 · 130 LouphesorlysLoughArgThrCysGluLeuIleTyiLeuIhiGluPinSerSer Ser 149 150 HeSerThrCluffeAsnSerAlaLeuValLeuLysValSerTrpHeThrPheLeuLeu 169 170 AlaLysGlyGluValLeuGlnMetGluAspAspLeuValIleSerPheGlnLeuMetLeu 189 110 SerThillysValAspAsnAlaMetSerArgLenLysLysTyrAspValLenPheAla 129 679 ATAICTACTGAAATAAATTCTGCATTGGTGAAAAGTTTCTTGGATCACATTTTTATTA 738 859 ACAGCIGTATACCCATFAAIGGITCACCTCGAACACCCAGGCGAGGTCAGAACAGGAGT 918 499 CAGAAAAAACATAGAAATCAGTGTCCATAAATTCTTTAACTTACTAAAAGAAATFGATACC 558 190 CysValLeuAspTyrPhelleLysLeuSerProProMetLeuLeuLysGluProTyrLys 230 AlaArqileAlaLysGlnLeuCluAspAspTbrArqileileGluValLauCysLysGlu 250 BisGluCysAsnleAspGluValLysAsnValTyrPPeLysAsnPeTieTroPheMet 270 AshSerfe0GlyReuValThrSerAshClyReuProGluValGluAshLeuSerfysArq 330 AshleuAspGluGluValAshVallleProProHisThrProValArqThrValMetAsh 350 ThrileGlnGlnLeuMetMetIleLeuAsnSerAlaSerAspGlnProSerGluAsnLeu 370 HeSerTyrPheAsnAsnCysThrValAsnProLysGluSerHeLedLysArqValLys 290 TyrGluGluIleTyrLeuLysAsnLysAspLeuAspAlaArqLeuPheLeuAspHisAsp 310 LysThrLeuGlnThrAspSerIleAspSerPheGluThrGluArgThrProArgLysSer 210 ThralaValileProlleAspSlySerProArqThrProArqArqClySluAshArqSer .159 AAAACTCTTCAGAGTGATTCTATAGACAGTTTTGAAACAAQAGAAGACCAAAAAAAAATT $\overset{\circ}{\circ}$ d õ qq ò å ò q ô qq ć ď ò q ô 5 ŝ d õ qq q ô d ò qq ŝ q ŝ q ò d ô

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                                                                                                                                                                                                                                                                                                                 FMM CLIAALLIAAAAGCCTTTGATTTTTACAAAGTGATAAGTTTTTATCAAAGGAGAGGC 1758
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2719 AGAAGTGCTGAAGGAAGCAACCCTCCTAAACCACTGAAAAAACTACGCTTTTGATATTGAA 2778
                                                                                                  850 GlySerAspGluAlaAspGlySerLysHisLeuFroGlyGluSerLysFbeGluGluLya 869
                                                Gene is taken from human chromosome 13g14 retinoblastoma (RH) conA. By installing a working USG, safe and specific treatment and prophylaxis can be given to cancer patients.
                                                                                                                          2779 GGATGAAGGAAGGAGATGGAAGTAAAGATGTGGGAGAGAGTGGAATTLIGAGGAGAA
                                                                                                                                                   870 LeuAlaGluMetThrSerThrArgThrArgMetGlnLysClnLysMetAsnAspSerMet
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        by replacing inellective cancer suppressing gene with ploned, active gene.
                                                                                                                                                                                                                                                                                                                                                                               Cancer; cancer supressing gene; CSG; 13q14; retinoblastoma;
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Conservative:
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                                                                                                                                                                                                    890 AspThrSerAsnLysGluGluLys 897
                                                                                                                                                                                                                                                                            AAQ04713 standard; cDNA; 2994
                                                                                                                                                                                                                                                                                                                                                        Cancer supressing gene (CSG)
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P-PSDB; AAR05305.
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5 :	4	AsplanProLauValArqlanGluPhaGluGluThrGluGluProAspPhathrAlalau	09
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5 3	<u>.</u>	Cystintystaetrystiefroksplisselandiandamaalaripileu 1914 H.H.H.H.H.H.H.H.H.H.H.H.H.H.H.H.H.H.H	76 378
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7.0	410	euGlaThrAspSerTleAspSerPheGluThrGlnArdThrProArgly	29

qo	1159	HERFELLER FELLER	1218
ζÒ	330	AsnLeuAspGluGluValAsnVallleProProBisThrProValArdTbrValMetAsu	4.5
qq	1219	AACCITGA IGAAGA GAAA IGTAATIT COT CCACACACACACTTAGGACTI GITA LGAAC	278
Oy	350	Thr LeGindinguMetMet HelenasnSerAlaserAspGinProserGluAsnLeu	6.9
qq	1279	ACTATCCAACAATTAATGATGATTTTAAATTCAGGAAGTGATCAACCTTCAGAAAATCTG	æ *
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a C	1339	ATITTCCTATITTTAACAACTGCACAGTGAATCCAAAAGAAACTATACTGAAAAGAGTGAAG	¥6¥
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qn	1399	GATATAGGATAGATCTTTAAAGAGAAATTTGCTAAAGCTGTGGGATAGGTTGTGTGGAA	458
ολ	410	TeGlyserClnArgTyrLysLeuClyValArgLeuTyrTyrArgValMetGluserMet	f. 7
qq	1459	ATTGGATCACAGGGATACAAACTTGGAGTTCGCTTGTATTACGAGTAATGGAATCCATG	518
ÓΫ	430	LeulysSerGluGluGluArdLeuSer11eGluAsnPheSerLysLeuleuAsnAspAsn	2.
qq	1519	CTTAAATCAGAAGAAGAAGAATTATTATTATTATTATTATTATTATTA	5.78
Oy	450	IlePheHisMetSerLeuLeuAlaCysAlaLeuGluValValMetAlaThrTy:SerArg	5.9
qu	1579	ATTITICALATICITITATIOGCOTOCOCITITOACOLICITATIOACACATATATA	6.38
ΟŸ	470	SerThrSerGinAsnicuAspSerGiyThrAspicuSerPheProTrp11cleusAshVal	ა დ
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Qy	490	LeudsniculysalaphedsphetyrtysValiteGluserphetletysAlachudry	60
qu	1699	CTTAATTTAAAAGCTTTGATTTTTACAAAGTGATCGAAAGTTTTATTAAAGTAGAGG	758
Óγ	510	AsnLeuThrArgGluMetlleLysHisLeuGluArgCysGluHisArgTleMetGluSer	6.7
90	1759	AACTTGACAAGAGAAATGALAAAACATTTAGAACGATGGAACATGGAATGATGT	8 3
OY	530	LeualaTrpLeuSeraspSerProLeuPheaspLeu11etysG1nSerLysaspArquin	2.4
qq	1819	CTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAAACAATCAAAGGACAGAAA	н7в
ОУ	550	GlyProThrAspHisleuGluSerAlaCysProLeudAsnLeuProLeuGlnAsnAsnHis	59
10 b	1879	GGACCAACTICATICAATGTGTTTGTCCTCTTAATGTTCCTCTCAGAATAATGAG	9.38
Qy	570	ThrAlaAlaAspMetTyrLeuSerProValArqSerProLysLysClySerThrThr	68
qu	1939	ACTGCAGCAGATATGT ATCTTTCTCCTGTAAGALCT CCAAAGAAAAAGGTT CAACTAGG	866
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qa	1999	CGTGTAAATTCTACTGCAAATGCAGAGAACACAACCTCAGCTTCCAGAACCAGAAG	058
οy	610	ProfeculysSerThrSerLeuSerLeuPhetyrLysLysValTy1ArqLeuAlatyrLeu	50
qc	2059	CCATTGAAATCTACCTCTTTCACTGTTTTAAAAAAGTGTATGGCTAGCTTTTTTT	<u>8</u>
Qy	6 40	ArgLeuAsnThrLeuCysGluArgLeuLeuSerGluHisProGluLeuGhuHis11e-11e-	6.4
q(I	2119	CGGCTAAATACACTTTGTGAACGCCTTCTGTGTGACACACAGAATTAGAACATATGT	178
oy.	059	Trp1hr1cuPheclinHisthr1cuGlnAsnGln1yrGluIcuMcrArqAsyArqHistcu POHTHILIH HILLIH	699
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J.	#157TF		63.83	ā	AAA23331	Human retinoblasto
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                                                                                                                                                                                                                                                                                                                                                                                  protein (RISP) of the invention. The proteins can be used for inhibiting callular proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases enhancherised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectum of
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        100.0%; Score 3347; DB 19; Length 3347; 100.0%; Pred. No. 0;
                                                                                                                               Retinoblastoma suppressor protein with N-terminal modification
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                                                                                                                                                              inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           0; Mismatches
                                                                                                                                                                                                                                                      laim 22; Fage 196 200; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     activity than wild type RTSPs.
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1: 1998-480788741.
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                                                                                                                                                                                                             901 GLAAFIGGIGGAGAGAGAGAGAGAGTGITAIGAACAGTATGCAACAATTAATGALG 960
781 AATAAAGATOTAGAAGATTATTITIGGATOATGATAAAAOTOTTOAGACTGATTOT 840
                                              781 AATAAAGATCTAGATGCAAGATTATTTTTGGAFGATGATAAAACTGTTGAGACTGFFGF 84U
                                                                                         841 ATAGACAG FITTGAAACACAGAGAACACCAGGAAAAAG FAAGG ITGATGAAGAGG GAAT 900
                                                                                                                                                                                                                                                                                                       1201 TTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTCATATGTCTTTATTG
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CTOTAGATAGATAGAACTCAFGAGAGAGAACATTTGGACCAAATTATGATGGTTCC ATCHATGATAGAACAGAACAGAACTTAGAACAAAATCAAAATTCAAAAATCAAAAATAAAAAAAA	TATAANGATCTTOCTCATGATGITOAGAGACATTCAAACGTGTTTTGATCAAGAAGA 	GAGTATGATTCTATTATAGTATTCTATAACTCGGTCTTCATGCAGAGACTGAAAACTAATTTTTTTT	ATH HOPAGIATOP HOPAGCAGO OCCIACO HIGGAGAATACCEGAGII IGGIGGA HELLELLI HILLI HILLI HILLI HILLI HILLI HILLI HILLI HILLI HILLI AFITHGCAGIATACCTGCAGCAGGCCCIACCTGTCACCAATACCTCACATICCTGGA	APPOTTA AAAGI FECTAGI FOACOTTAOGATFOCTGGAGGAACAFCEATATFOA TELLELLELLELLELLELLELLELLELLELLELLELLELL	CCCCTGAAGAGTCCATATAAAAFTTCAGAAGGTCTGCCAACACCAACAAAATGACTCCA DTLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL	APARCAADAATETTAGTATCAATTOGTGAATCATTOGGGACTTCTGAGAAGTFCCAGAAA 	ATAAATCAGATGGTATGTAACGGCGGTGGTGCTCAAAAGAAGTGCTGAAGGAGCAAC 	CCTCCTAAACCACTGAAAAAACTACGCTTTGATATTGAAGGATCAGATGAADAAGGA 	AUTAAACATCTCCCAGGAGGAGTCAAATTTCAGGAGAAACTGGCACAAATGACTTCTACT TTTLLTTTTTTTTTTTTTTTTTTTTTTTTT	CGAACACGAATGCAAAAGCAGAAATGAATGATAGCATGGATACCTCAAACAAGGAAGG	AAA IGAGBATCT CABAACCT GGTGGACACTGTGTA AACCTCTGGATTCATTGTCTCAAAATGAGGAGATCTCT CAAATGAGGAGACTTGGGTGGACACTGTGTGTCTCTCAAATGAGGATCTCT CAGACCTTGGTGTCTTCATTGTCTTCATTGTCTTCAT	CAGA GORGA GO A DA AGO O CORONA DE CONTRA GORGA O DA AGADA GORGA DE LA COMPANA DE COMPANA DE COMPANA CONTRA COMPANA CONTRA CONTRA COMPANA CONTRA CONT	CTTTTTGTGGGTAFAAAATGTGCAGATGGTTGGGTGGGTGATFCGACTGAAA ELLILLILLILLILLILLILLILLILLILLILLILLILLI	AFGITAGICATIGITATITATACAAGATIGAAAATCITGIGAAAATCCTGGCATTTAAAA 	AUTHOLANCAGA DOLLOCIC LICGAAAGTAAAAT KOOLGOOCTTALOGALAGAAGAAAAA LICLICILLI LILLILLILLILLILLILLILLILLILLILLILLI	ATOR CCTAGACTOROACTCCTGATAACCAGACCTGACTACTACTTGCTTCTG	TAGGATATAGGTGATGTTTGGTTTTTATAATTTATATGGTATATTTTAATTT
1861 1921 1921	1381	2041	2101	2161	2221	7.2H]	2441	2401	2461 2461	2521	2581 2581	2641	2701	2761 276.1	28.21 28.21	2881	2'941
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3001 AACATGAACACCCTTAGAAAATGTGTCCTALCTTCCAAATGCAATTGATTGACTG 3060
                                                3061 CCCATTCACCAAAATTATGCTGAACTCTTGTGCAAAAATGGATATTATTAGAAATTAGAA 3120
                                                                                                                               3061 CCCATTCACCAAAATTATCCIGAACICIICIGCAAAAAIGGATAIIATIAGAAATTAGAA 3120
                                                                                                                                                                                                                                3181 GCTTGTTTTATAAAALTTTTGCTTTTAATTAAATAAAAGCTGGAAGAAAAGTTATAAATA 3240
                                                                                                                                                                                                                                                                                               3241 TGATACTATCATACTGAAACAGATTTCATACCTCAGAATGTAAAAGAACTTACTGAT 3300
                                                                                                                                                                                                                                                                                                                  3121 AAAAATTACTAATTTTACACATTAGATTTTATTTTACTATTGGAATCTGATATACTGTGT 3180
                                                                                                                                                                3121 AAAAATTACTAATTTTACACATTAGATTTTAATTTTACTATTGGAATCTGATATAAGT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                               3301 TATTTTTTTCTTCATCCAACTTATGTTTTTAAALGAGGALLAFTGALAGT +347
                                                                                                                                                                                                                                                                                                                                                                                 3301 TAFTTTGTTGATCGAAGTTATGTTTTAAATGAGGATTATTGATAGT 447
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Modified retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Claim 22; Page 226 230; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     cellular proliferation inhibitor; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Location/Qualitiers
7...2793
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Ha S, Xa H, Zhou Y;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  AAV58452 standard; DNA; 4554 BP.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 (BAYU ) BAYLOR COLLEGE MEDICINE.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  (TEXA ) UNIV TEXAS SYSTEM
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               WPI; 1998-480788/41.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   P-PSDB; AAW69376.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Benedict WF,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  19-FEB-1998;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Homo sapiens
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×χ	Sergie	puence 3554 BP; 1170 A; 683 C; 653 G; 1048 T; 0 other;	
) ž :	Berg M. est Loc	93.4%; Score 3126.8; DB 19; Length 3554; 94.1%; Pred. No. 0;	
ξ ζ	5	SS#S) CONSEINALINE UT MISMALCHES D. THACLS 201, CAPS I) CACHTEATHAR AND MANAMANANA AND AND AND AND AND AND AND AND AN	
ą	-	UTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	
숙흥	3 7	GAACCCCGGGCACGGCGCGCGCGCCCCCCGGAGGAGGCCAGAGCAGAGCGGGC 120 FILETELLETELLETELLETELLETELLETELTELTELTELLETELTEL	
F 8	121	PORGAGOACTICICICALCAROCTICACITICACITICAGAGAGAGAGAGAGCIGATITIACT 	
숙 후	<u> </u>	GCATTATGTCAGAAATTAAAGATACCAGATCATGTCAGAGAGAG	
÷ 4	241		
5 3	401		
Ś	14.2	34	
ē	3.6.1	GAGCTATAGAAAAACATAGAAAFGAGTGFCCATAAATTCTTTAACTTACTAAAAGAAATT 42	
S	7.4.7	341	
ą	4.21	SATACCAGTACCAAAAGTTGATAATGCTATGTC	
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ź	4 H J	TTTGCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATATTTGACACACCCAGC 540	
b 3	44.2 54.1	AICIACTGAAATAAATTCTGCATGCIAAAAGIIICIISGAICACAIIT 393 	
なぜ	43. 11.3	TTATTAGETAAAGGGGAAGTATTACAAATGGAAGATGATGGTGGTGATTTCATTTCAGTTA 453 	
황물	454	AUGCIAIGIGCHGACTAITTIAITAAACTGIGAGCHGTTGCTGAAGAACA 513 HILLHIHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	
÷ €	514	TATAAAAGGGGGGAGGTGAATGATGGTTCACCTCGAACACCCAGGCGAGGTCAGAAC 573 	
\$ ±	781	AGGAGIGCACGATAGCAAAACAACTAGAAAATGATACAAGAATTATTGAAGTTCTCTGT 633 	
等 畫	रू 1 क	AAAGAA?TIGAAIGIAATAIAGAIGGAGGGAAAAATGTTTATTTGAAAAATTTTTATACCT 693 FILLIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	
\$ 2	44.4 10.6	TITATGAATTCTCTGGACTTGTAACATCTAATGGACTTCCAGAGGTTTGAAAATCTTTCT 753 FILLEFFEFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	
÷	754	AAACGATACGAAAAATTTATCTTAAAAATAAAGATCTAGATGCAAGATTATTTTGGAT 813	

qq	961	AAAGGATAGGAAATITATGTTAAAAATAAAGAIGTAGATGGAAGATATTTTGGAT 10	1020
ÓΫ	814	CATGATAAAACUCTTCAGACUGATTCTATAGACAGTTTTTGAAAAAAAGAAGAAGAAGAAGA 87	873
1 2	1021	CATGATAAAACTGTTCAGATTGTTGTATAGACATTTTTGAAACACACAGAGATTTTTTTT	1080
Οy	874	AAAAGIAACCIIGAIGAAGAGGIGAAIGIAAAITCCICCACACACICCAGIIAGGACIGII 9	933
qu	1081	AAAAGTAACCTTGATGAAGAGGTGGATGTAGTTGCTCCACACACA	1140
Oy	934	934 AIGAACACTATCCAACAATTAATGATGATTTTTAAATTGAGGAAGTGATGAAGCTTGAGAA 993	866
qq	1141	ATGAACACTATCCAACAATTAATGATTTIAAATTCAGCAAGTGATCAACCTTCAGAA 12	1200
ØΣ	994	AATCEGATTECCTATTTTAACAACTGGACGGGATGCAAAGAAGAAGTATACTGAAAGA LU	1053
UP	1201	AATCTGATTTCCTATTTTAACAACTGCAGAGTGGAATGCAAAAGAAAG	1260
Óγ	1054		1113
d:	1261	GTGAAGGATAGGATAGATGTTTAAAGAGAAATTTGGTAAAGGTGTGGGAGAGGGTGT	1320
Οy	1114	GTCGAAATTGGATGAGAGGGATAGAAGTTGAAGTTGGGTTGTATTAGGGAGTAATGGAA 11	1173
qa	1321	GTCGAAATTGGATCACAGGGATACAAACTTGGAGTTCGCTTGTATTACCGAGTAATGGAA 13	1380
ΟY	1174	PCCATGCTTAAAFCAGAAGAAGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAAT 12	1233
qu	1381	TCCATGCTTAAATCAGAAGAAGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAAT 14	1440
Q	1234	GACAACAITIICAIAIGETIIAITGAGAGAGAGATGIIGAGGATGIAATGGGCACATAT 1.	1293
qu	1441	GACAACATTTTTCATATGTCTTTATTGGCGTGCGCTCTTGAGGTTGTAATGGCCACATAT 15	0051
ΟŸ	1294	AGGAGAAGTAÇATCTGAGAATCTTGATTCTGGAACAGATTTGTTTTGCATTGCATTGTG 13	353
qa	1501	AGGAGAGATACATCTCAGAAFCTTCATTCTCGAACAGATTGGTGTTCCCATGGATTCTG 15	0951
ΟY	1354	AATGTGCT/FAACT/F/AAAAGCCT/FTGATT/F/TACAAAGTGATCGAAAGT/F/FFT/FAT/CAAAGCA 14	1413
qn	1561	AATGTGCTTAATTTAAAAGCCTTTGATTTTTTACAAAGTGATCGAAGTTTTTATCAAAGCA 16	1620
Qy	1414	GAAGGTAACTTGACAAGAAATGATAAAAACATTTAGAAGGATGTGAACATCGAATGATG 14	1473
qo	1621	GAAGGCAACTTGACAAGAAATGATAAAAGATTTAGAAGGATGTGAACATCGAATGATG	0891
Οy	1474	GAATGCCTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAAACAATCAAAGGAC 15	533
d d	1681	GAALGCCTIGCAIGGCTCTCAGATTCACCTTATTIGATCTTATTAAACAATCAAAGAC 17	1743
Qy	1534	CGAGAAGGACAACTGATGACCTTGAATCTGCTGCTGTTAATCTTGCTGTGCAGAA! !:	863
qu	1741	CGAGAAGGACCAACTGATCACCTTGAATCTGCTTGTCCTCTTAATCTTCCTCTCTCCAGAAT 1E	800
ογ	1594	AATCACACTGCAGAGATATGTATCTTTCTCCTGTAAGATCTCCAAGAAAAAAGGTTCA 16	1653
qu	1801	AATGAGAGTGGAGGAGATATGTTTTTTTTTTTTTTTTT	1860
ΟY	1654	ACTACCOTOTAAATTCTACTGCAAATGCAGAGACACAAGCAACCTGCAGAGCTTCAGAGCC 17	713
a Dig	1861	ACTACGERITANATICIANTERANTERAGASAN ACAMGERACETERAGE TOTAGAS OF 19	1920
Οy	1714	CAGAAGCCATTGAAATCTACCTCTTTCACTGTTTTATAAAAAGTGTATGGGCTAGCC 17	773
q ₀ ,	1921	CAGAAGGATTGAAATCTACCTCTTTCACTGTTTATAAAAAGTGTATCGGCTAGCC 19	086
δ . :	1774	TATCICCGGCIAAATACACTIIGIGAAGGOTTGTGTGTGAGGAGCAGGATAGGAGAT 18	.833
q a	1981	TATGTGGGGCTAAATACACTTTGTGAACGCCTTGTGTGTG	2040
0y	1834	AICATCIGGACCCTTTCCAGCACCTGCAGAATGAGTATGAATCATGAGAGAGA	8683
qq	2041	ATCATCTGGACOCTTTTCCAGCACACCTGCAGAATGAGTATGAATTCAACTCATGACACACAC	2100

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This sequence encodes a modified retinoblastoma tumour suppressor
protein (FMSP) of the invention. The proteins can be used for inhibiting
cellular proliferation, when coadministered with a p53 protein. The RISIS
can be used for treating diseases characterised by abnormal cellular
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                                                                                                                                                              1213
                                                                                                                       3421 AAAAGCTGGAAGCAAAGTATAACCATATGATACTGATACTGAAACTGAAAGAGATTLCATA 3480
                                                                                                                                                                                                                                                                                 3181 TAATITATATGIATATTITITAATTIAACATGAACACCCTTAGAAAATGTGTGTTATGT 3240
                                                                   3214 AAAAGCTGGAAGCAAAGTATAACCATATGATACTATCATACTGAAACAGATTTCATA 3273
                                                                                                                                                                                                                                                                   3274 CCTCAGAAIGTAAAAGAACTTACTGATTATTTTCTTCATCCAACTTATGTTTTTAAATGA 3334
                                                                                                         3094 AAAAATGGATATTATTAGAAATTAGAAAAATTACTAATTTTACAATTTAGATTTATT
3034 ATCTTCCAAATGCAATTTGATTGACTGCCATTCACCAAAATTATCCTGAAATTGTCTC
                                                                                                                                                           Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Modified retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Disclosure, Page 121-126, 249pp, English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Location/Qualitiers
                                                                                                                                                                                                                                                                                                                                                                                                                   AAV58440 standard; DNA; 3555 BP.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                     02-DEC-1998 (first entry)
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proliferation, particularly cancers. The RTSPs have a broader spectrum of activity than wild type RTSPs. - FILLER FELLET 2.2) GIGGAGGARGAPOTGOTTOTTOGET AGGITT AGGITT AAAAAAAAAAAAAAAAAGAAGATTTTAGT 180 GAGAAAG111CATCTGTGGATGGAGTATTGGGAGGTTATATTCAAAAGGAAAAGGAACTG 300 634 ITIATGAATTCTCTTGGACTTGTAACATCTAATGGACTTCCAGAGGTTGAAAATCTTTCT 753 (+) GAGCTACAGAAAACATAGAAATCAGTGTCCATAAATTCTTTAACTTACTAAAAGAAATT 420 121 GAIACCAGIACCAAAGITGATAAIGCTAIGICAAGACIGIIGAAGAAGIAIGIAIIG 480 181 111GCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATTTTGACACAACCCAGC 540 *42 -----ATCTACTGAAATAAATTCTGGGTGCTAAAAGITTCTTGGATGAAAA3 541 AGLICGALAICTACIGAAATAAATTCTGCATTGGTGCTAAAAGTTTCTTGGATCACATTT 600 601 ITATTAGCTAAAGGGGAAGTATTACAAATGGAAGATGATCTGGTGATTTCATTTCAGTTA 650 4/4 AIGGIAIGIGECTEGACTATITALIAAAPEEEGGGGGTGGTGCTGAAGAAGAAGA 513 514 TATAAAACAGCIGTTATACCCATTAATGGTTCACCTCGAACACCCAGGCGAGGTCAGAAC 573 574 ACCAGTGCACGCATACCAAAACAACTAGAAAATGATACAAGAATTATTGAAGTTTCTCTCTGT 633 781 AGGAGTGPACHGATAGPAAAAPAACTAGAAATGATACAAGAATTATTGAAGTTGTGTGT 840 841 AAAGAACATGAATGTAATATAGATGGTGAAAAATGTTTTGAAAAATTTTGAAAAGT 2; Indels 207; Gaps 93.4%; Score 3126.8; DB 19; Length 3555; Sequence 3555 BP; 1171 A; 684 C; 653 G; 1047 T; 0 other; 401 FGGGGAATGTGTTTTTTTGCAGCTTGACCTAGTGGA--Pred. No. 0, 0; Mismatches 94.18, Matches 3345; Conservative Similarity = ŝ £ 5 Ś 5 Ē Ē £... ŝ 3 5 Ĭ

994 AATCIGALITICCTATITIAACAACIGCACAGIGAAICCAAAAGAAAGTATACIGAAAAAA 1053 1054 GTGAAGGATATAGGATACATCTTTAAAGAGAAATTTGCTAAAGGTGTGGGACAGGGTGT 1113 1114 GTOGAAATTGGATGAGAGATAGAAAGTTGGAGTTGGCTTGTATTAGGGAGTAATGGAA 1173 1321 GTCGAAATTGGATCACAAGATACAAACTTGGAGTLCGCTTGTATTACCGAGTAATGGAA 1380 1174 TCCATGCTTAAATCAGAAGAAGGATTATGCATTCAAAATTTTAGGAAACTTCTGAAT 1233 1234 GACAACATTTTTCATATGTCTTTATTGGCGTGCGCTCTTTGAGGTTGTAATGGCCACATAT 1293 1294 ACCAGAAGTACATCTCAGAATCTTGGAACAGATTTGTCTCTTTTGTCTTTTGT 1353 961 AAACGATAGGAAATTITATGITAAAAATAAAGAICIAGAIGGAAGATIATITITGGAT 1020 1081 AAAAGTAACTIGAIGAAGAGGAAIGIAAIICCICCACACTCCCAGIIAGGACIGII 1140 1261 GEGAAGGATAFAGGAFACTETTAAAGAGAAAATTEGTAAAGCTGTGGGACAGGGTTGT 1320 1501 AGCAGAAGTACATCTCAGAATCTTGATTCTGGAACAGATTGTGTTCCCALGGATTCTG 1560 1414 GAAGGTAACTTGACAAGAAAIGATAAAACAITIAGAACGATGTGAACATCGAATCATG 1681 GAATGGGTIGGATGGGTGTGGGATTGACGTTTATTTAATTAAACAATGAAAGGAG 1740 1594 ANTONOMOROMACAGATATGIANOTINICICISTAAGAICICCAAAGAAAAAAGGINGA 1653 1714 CAGAAGCCATTGAAATGTAGGTGTTTGACTGTTTATAAAAAAGTGTATGGGCTAGCC 1773 1774 TATCTCCGGCTAAATACACTTFG GAACGCTTCTGTCTGAGGCACCCAGAATTAGAACAT 1833 754 AAACGATACGAAGAAATTTATCTTAAAAATAAAGATCTAGATGCAAGATTATTTTGGAT 813 874 AAAAGTAACGTIGATGAAGAGGTGAATGIAATTGCTGGAGACACTCGAGTTAGGACTGTT 933 934 ATGAACACTATCCAACAATTAATGATCTTTAAATTCAGCAAGTGATCAACCTTCAGAA 993 814 CATGATAAAACTCTTCAGAGTGATTCTATAGACAGITITGAAACACAGAGAACACCAGGA 873 1981 TATCTCCGGCTAAATACACTTTGTGAAGGCCIICTGTGAAGAGCAGCCAGAATTAGAAGAT ... **q**□ : ô ò ò ద $^{\circ}$ g ò QCI q qq d g 감 δ οy ò Ş ó 5 ò 9 Ś 5

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0.9 1894 0.9 1894 0.0 1954 0.0 2161 0.0 2014 0.0 2021	2281 2144 2194 2401 2254 2461 2314 2521	2374 2581 2641 2641 2701 2554 2761	26.14 26.74 26.74 27.44 27.44 27.44 27.94 3001 28.54 3001 28.54

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                                                                                                                                                                       3121 CCIGICIGACTACTTIGCCIICTITTGTAGGAALALAGGAALGIILOGIGIIGIIIIA1 3180
                      2974 TAATITATATGTATATITITAATITAACATGAAGAGGGGGTTAGAAAATGTGTGTGTCT 3033
                                                                                                               3094 AAAAATGGATATTATTAGAAATTAGAAAAAAATTACTAATTTTAGACATTAGATTTTATT 3153
                                                                                                                                     3274 CCTCAGAATGTAAAAGAACTTACTGATTATTTTTTTCATCCAACTTATGTTTTTAAATGA ++3+
                                                                                                                                                                                                                                                               Minimal promoter; tetracycline responsive expression vector; TREV;
                                                                   3034 ATCTTCCAAATGCAATTTGATTGACTGCCATTCACCAAAATTATCCTGAACTTCTTGC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 New tetracycline responsive expression vectors - used for the tightly controlled expression of genes, such as tumour suppressor genes for treating cancers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                transcriptional transactivation domain; 140;
tetracycline repressor protein; TRP; tetracycline operator;
production; stable cell line; protein production;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 tumour suppressor protein; treatment; caucer; ss
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                                                                                                                                                                                                                                                                                                                                                                                                                                                 DNA sequence of the specification
                                                                                                                                                                                                                                                                                                                                                                             AAV54990 standard; DNA; 3555 BP.
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Disclosure; Pages 145-150; 190pp; English

The present acquered appears in the specification, which describes a retracycline responsive expression vector (TREV), which contains a sequence encoding a luston protein comprising a transcriptional transactivation domain (TTD) operatively attached to a tetracycline repressor protein (TRD), the first sequence operatively positioned downstream of a promoter. The vector also contains a cloning site operatively positioned downstream of a basal promoter comprising a leracycline operator. The TREVS can be used to produce stable call ince in which gene expression is tightly restained by tetracycline. They can be used for treating diseases characterised by shoromal collular proliferation, particularly cancers.

FITH HITTELLITE HITTEL 12] COGGAGGASCITCTCTCTCTCTCACGCTTGACTTGAAGAAACAGAAGCTGATTTAACT 180 18) CONTINITATOR CANANTA AND A CONTINITA A CARACTAR A CARACTA CANTA A CARACTA 241 GAGAAGITIGALGIGGALGGAGIAITGGGAGGITAFATICAAAAGAAAAGGAACIG 300 241 GAGAAAGTTTCATCTGTGGATGGAGTATTGGGAGGAGTTATATATTCAAAAGAAAAAAGAAACTG 300 30] TGGGGAATCTGPATCTTTAFFGCAGTAGTFGACCTAGATGAGTGTGGTFCACFFTTACT 360 361 GAGCTACAGAAAAACATAGAAATCAGTGTCCATAAATTGTTTAAGTTACTAAAAATT 420 4.2.1. CATACCACTACCAAAGTTGATAATGCTATCTAAAACTGTGAAAACTGAAGAAGTGTATGATGTTG 4.80 48] HIIGCAM FOLLIMAGMAAATHGGAAAGGAMAHGTGAAAGTTATATATTTGAAAAGGGAGG 540 · · · · · · · ATCTACTGAAATAAATTCTGCATTGGTGAAAAAGTTTCTTGGATCACATTT 393 541 AGTICGAIAICTACTGAAATAAATICTGCATTGGTGCTAAAAGTTTCTTGGATCACATTT 600 394 T.A.L.HARCHAAAGGGGAAAGTATTACAAATGGAAGATGATCHGGRGAFFTCAFTCAFTFCAGFTA 453 601 IIAITAGGIAAAGGGGAAGTATTACAAATGGAAGATGATGGGTGATTOATTPVAGTTA 660 454 ATGCTATGTGTGTGTGTATTTGATTAAAGTGTGAGCTGCCATGTTGCTGAAAGAACCA 513 65] ALGCIALGEGICCTTGACTATTTTAAACTCTCAACGAGGTGCTGAAAGAACQA 720 574 AGGACTGCACGGATAGCAAAACAACTAGAAATGATACAAAAHTATTGAAGTTGTGTGT 633 2; Indels 207; Gaps 93.4%; Score 3126.8; DB 19; Length 3555; 94.1%; Pred. No. 0, by abnormal collular proliferation, particularly cancers. Sequence 3555 BP; 1171 A; 684 C; 653 G; 1047 T; 0 other; ----ASSTOTOTOTITIVITATIONAGINAGITIAAOITAGIGGA----0; Mismatches Conservative Similarity 342 -----Matches 3345; Query March 3 Ē Š $\tilde{\Xi}$ 5 â Š. 2 ć â š $\bar{\Xi}$ 5 3 ŝ ŝ ŝ ŝ Ξ 3

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hEST2; telomerase, catalytic subunit, reverse transcriptuse, life span;
retinoblastoma; p53; tumour suppressor; inhibitor; afferioselerosis;
proliferation; immortal; tumour therapy; macular degeneration; activator;
            2854 AATTGCTGTGCTTTTATGGATAGTAAGAATGGCCCTAGAGTGGGAGTCCTGATAACCAGG 2913
                                                        3121 CCFGFCTGACTACTTTGCCTTCTTTGTAGCATATAGGTGATGTTTGCTCTTGTTTTAT 3180
                                                                                                                                                   3034 ATCTT CCAAATGCAATT GATTGCCCATTGACCAAATTATGCTGAACTGTTGTG 3093
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17-FEH-1999;
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New method for increasing the proliferative capacity of cell lines comprises administering agents reversibly activating telemerase activity and reversibly inactivating Rb/INN4 and/or p53 pathways useful in treating age related diseases

Maim 5: Page 121 123; 123pp; English.

The invention concerns methods and reagents for extending the life span, e.g., the number of minolic divisions, of a cell. The method relies on a circation of a telemental activity and inhibition of one or both of a critadian of a telemental activity and inhibition of one or both of a retinoblastona (Rb)/INK4 pathway or a p53 pathway, phosphorylation of Rb by cyclin-drependent Kinases, edk4 and edke. The leases the cells into the division cycle. Hinding of INK4 family members, e.g. the tumour supressor suppressor plaimathaters can selectively and results in growth arrest. Rb inactivators can selectively and reversibly inactivate and an Figure and activity and results in growth arrest. Rb inactivators can selectively and the p53 tumour suppressor and corn also be used in the marchale function and the p53 tumour suppressor and corn also be used in the marchale which can be used in the marchale which by the residues K22. F24. H95 and/or p77. Additional constructs include a papilloma vitus E7 protein, or other viral oncoprotein which bypasses Rb and/or p53. Antisetse constructs of the Rb and p661NK44 genes may also be used. The methods are useful for increasing the proliferative capacity of cells. The cells are used to treat conditions related to (premature) agains, e.g. macular degeneration and arteriosclerosis. The cells can also be used to replace tumour cell lines in vitro and lor studies on biochemical and cosmette dispersed thmour cell lines in vitro and lor studies on biochemical and physiological aspects of no profession of normal or genetically engineered

Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other;

301 122 COGAGGACCTGCCTCTCAGGCTTGAGTTTGAAGAACAGAAGCTGATTTTACTG 181 55 + ATACCAGTACOAAAGITGATAAIGCTAIGTCAAGACIGTIGAAGAAGAAGTAIGAIGIAITGI 612 Gaps 19.1. AUGI AGAAAAAAGATAGAAATCAGTGTCCATAAATTCTTTAACTTAAAAGAAATTG 93.4%; Score 3125.8; DB 21; Length 4839; 94.1%; Pred. No. 0; 2, Indels 207, 102 GGGGAAIGTGTATTGCAGCAGTTGACCTAGTCGA-----0; Mismatches Conservative Local Similarity Matches 3344; Querry Match 37 5 Š <u>a</u> Š Ś 5 ŝ

1093 AACGATACGAAGAAATTTATCTTAAAAATAAAGATCTAGAIGCAAGATTATTTTGGATC 1152 1273 TGAAGACTATOOAACAATGATGATGATGATTOAAATTOAGAAGATGATGAGGTTGAGAAA 1055 TGAAGGATATAGGATACATCTTTAAAGAGAAATTTACTAAAAGGTGGGGTGTGT 1114 1393 TGAAGGATATAGGATATATTTAAAGAGAAATTTGATAAAGTGGGGGAACAGGGTGTGTG 1452 1115 TCGAAATTGGATGAGAGAGATAAAAGTTGGAGTTGGTTGTATTAGGGAGTAATGGAAT 1573 ACAACAITIIICAIAIGICIIIATIGAGAIGOSOIGITOAASITIGIAATGGOOGAAATAA 1632 1295 GCAGAAGTACATCTCAGAATCTTGATTCTGGAACAGATTTGTCTTTCCCATGGATTCTGA 1354 1633 GCAGAAGTACATCTCAGAATCTTGATTCTGGAACAGATTTGTCTTCCCATGGATTCTGA 1632 1355 ATGTGGTTAATTTAAAAGGGTTTGATTITTAGAAAGIGATGGAAAGTTTTATGAAAGGAG 1414 1033 ITARGAMITOTOTOGRATIOSTAAOATOTAATGBADITOGAGAGGIIGAAAATGITICIA 1092 755 AACGAVAGAAAATTIATCTTAAAAATAAAGAYCYAGAYGCAAGATTATTIYYGCATG 814 695 TIATGAATTOTOTGGAOTTGIAAGAICTAATGGACTTCCAGAGGTGAAAATCTTTCTA 754 815 AIGATAAAACICIICAGACIGATICIATAGACAGITTTGAAACACAGAGAACACAGAGAA 874 875 AAAGIAACCIIGAIGAAGAGGIGAATGIAAJICCIGCAGACICCAGIIAGGACIGIA 934 613 THGCACTCTFCACCAAAFFGGAAAGGACATGFGAACTTAFAFATATGACACAACCCAGCA 672 673 GTTCGATATCTACTGAAATAAATTCTGCATTGGTGCTAAAAGTTTCTTGGATCACATTTT 732 793 TGCTA IGLO MACTITGACTATITATIAAACTOTOAGCIOCCATGTIGCTCAAAGAAGGA 852 575 GGAGTGCACGGATAGCAAACAACTAGAAATGATACAAGATTATTGAAGTTGTGTGTA 634 635 AAGAACATGAATGTAATATAGAGGGAAAAAAIGIIIALIICAAAAAITIITALAGGII 694 ATCTACTGAAATAAATTCTGCATTGGTGCTAAAAGTTTCTTGGATCACATTTT 394 395 IATTAGCTAAAGGGGAAGTATTACAATGGAAGATGALGGGGGTTCGATTCATTCAGTTAA 454 455 ISSTATSTSTSCIISACIAIIIIAIIAAACICICACCICOCAIGIIGCICAAAGAACI 514 515 ATAAAAGAGTGITATAGCCAITAATGGITCACTCCAACACCAGGGGGGGGGCAACA HER ATAMANING TOTTATACO NITANIGHTO NO TORANINO CACOCACOCACOCACA 935 TGAACACTATCCAACAATTAATGATGATTTTAAATTCAGCAAGTGATCAACCTTCAGAAA 1175 CCATGOTTAAATCAGAAGAAGAACGATTATCCAATTCAAAATTTTAGGAAACTTCTGAATG 1453 TCGAAATTGGATCACGGGATACAAACTTGGGTTGGCTTGTATTACCGAGTAATGGAAT . . ŏ qq qq dG. 5 οy QQ Ω̈́ ò QO

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1415 AAGGTAACTEGATAAGAAALGATAAAACALIIAGAACGAIGTGAACATCGAATCATGG 1- 1754 AAGGTAACTEGATAAGAAATGATAAAACALIIHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	95 ATTATACTOTAGCADATATGTATCTTTCTCCTGTAAGATCTCCAAAGAAAAAAGGTTCAA 1 BELLIETTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	GAACGCTPTGTCTGAGCCTACAATTAGAACATA 1 GAACGCTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	1955 FTAAATTCAAAATCATTGTAACGATGCTCCCCCTCCTCTTCCCCGGGGCAT 229 TTAAATTCAAAATCATTGTAACGATGCTAGGGATCTTCCTCCTCGTCTTTTTTTT	HOTE AND AND TOWN TO AND THE CONTROL AND AND THE CONTROL AND T	THE CANCE AND THE CANCER AND THE CAN
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Rb; androgenic; antiandrogenic; identification; prostate cancer; ss.
                                                                                                                              2615 TACACCICTGGAITCATTGTCTCTCACAGAIGIGACIGIAIAACTIFCCCAGGTTCTGTT
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                                                                                                                                                                                                              AA288444 standard; cDNA; 4839 BP
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493 AGCTACAGAAAAANATAGAAATCAGTGTGCATAAATTCTTTAACTTACTAAAAGAAATTG 552
                                                                              553 ATACCAGTACCAASTIGATAATGCTATGTCAAGACTGTTGAAGAAGTATGATGTTATTCL 612
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Novel androgen receptor-associated proteins used to detect androgenic
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        The present sequence encodes a human androgen receptor coactivator
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        [H2] CATTATGTCM3AAATTAAAGATAGCAGATCATGTCAGAGAGAGAGAGTTGGTTAACTTGGG
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                                                                                                                                        /note= "androgen receptor coartivator"
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2713 TCANAAGAAGTGCTGAAGGAAGCAACCCTCCTAAACACTGGAAAAACTA'GCTTTGATA 2772
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Human, cancer, colon, breast, ovary, ocsophagus, kidney, thyrold, stemach, huby, prostate, pareteas, carcinoma, antitument, cancerous, cyristria, tebe therapy, actions/lastic, Wilm's tuneur, adenocareinema,
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                                           Breast cancer related gene sequence SEQ ID NO:1210.
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anti neoplastic agent. The method involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, determining a change in superssion of at least one gene (1) of a signature gene set, where (1) comprises a sequence (5) selected from 844? sequences (given in AHG1664 to ABU7010), or is at least 95% identical to (8), where a change in expression is indicative of out neceptastic activity. (1) has evicatally an anti-neoplastic agent, and can be used tor producing a product which is the data collected with respect to the anti-neoplastic agent as a sufficient to convey the chemical structure and/or properties of the agent. MI can be used in the treatment of cancer such as colon, breast, stometh, lung, thyrold,
                                                                                                                                                                                                                                                                                                                                                                                                                                      oesophageal, ovarian, kidney, prostate or pancrealic cancer, adenocarcinoma, carcinoma, clear cell cancer, infiltrating ductal cancer, infiltrating lobular cancer, squamous cell carcinoma, neuroendornine
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94.18; Pred. No. 0;
Live 0; Mismatches 2; Indels 207; (
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 carcinoma, papillary carcinoma and Wilm's tumour.
Claim 1; SEQ 1D 1210; 44pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Matches 3344, Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Local Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   342 -----
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_	-	ATCACACTGCAGCAGATATGTATCTTTCTCGTAAGATGTCTCCAAAGAAAAAGGTTCAA
	Oy 1655 Db 1993	655 CTACGCGTGTAAATTCTACTGCAAATGCAGAACCAACCACCTCAGCCTCTCAGACCTTTTTTTT
	· .	AGAAGCCATTGAAATCTACTCTTTTACTGTTTTATAAAAAGTGTATCGGGTTACCC
_	~	AGAAGCATTGAAATGTAGGTGTTTTTTTTTTTTTTTTTT
	-	ATCTCGGGTAAATACACTTGTGAACGCTTGTGTGTGTGAGCACCAGAATTAGAACATA
,	7	ATCHCCCCTAAATACACTITGTGAACGCCTTCTGACCACCCACAATTACAACATA
	OY 1835 Db 2173	PCATCTGGAGCCTTTTGCAGCATAGCAGCATAGAGTAGAATAGAATATAGAAAAAAAA
<u> </u>	Oy 1895	ATHTGGACCAAATHATGATGTGTTCALGTATGGGATATGCAAAGTGAAGAATATAGACC
_	Db 2233	APTEGGACCAAATRIGATGTGTTCCATCTATGCAACAACAACAACAATAATACAATAATACAACAATAATACAATAAT
	uy 1955	TTAAATTCAAAATCATGTAACAGCATACAAGGATCHFOTTCATGGGGGGTT-GGGGGGGGTC-TAGGAGACACAT
=	7	TTAAATTCAAAATCAFFGTAACAGCATACAAGGATCTTCCTCATGCTGTTCAGGACAT
- '	Oy 2015	TCAAACCTGTTTTGATCAAAGAAGAGGAGTATGATTGTTTTTTTT
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_	Oy 2075	TCTTCATCACCACAGACTGAAAACAAATTTTTCCAGTATGCTTCCACTAGGCCCCTAACT [[] [] [] [] [] [] [] [] [] [] [] [] []
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Ŭ	Oy 2255	TGCCAAGACCAACAAAAIGACTCCAAGATCAAGAATTTIATTAATTAATTAATTAATTAATTAATTAATT
_	2	TGCCAACACCAACAAAAATGACTGCAAGATGATTATTTTTTTT
J	Qy 2315	TCGGCACTTCTCAGAAGTTCCAGAAAATAAATCAGATGGTATGTAACAGGACCGTGTGC
_	7	TCGGGACTTCTGAGAAGTTCCAGAAATAAATCAGATGTATGT
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_	Db 2713	TCANAAGAAGTGCTGAAGGAAGCAACCCTCCTAAACCACTGAAAAACTACGTTTGATA
_	2	TTGAAGGATCAGATGAAGCAGATGGAAGTAAAATATCTFCCAGGAGGCTGCAAATTTTAGG
	2	THGAAGGATCAGATGAAGGAAGTAAAAAALCHCCAAGAGAGTAAAATTTAAGT
Ü	7	AGAAACTGGCAGAAATGACTTCTACTCGAACACGAATGCAAAAGCAGAAATGAAA 255
_	~	AGAAACIGGGAGAAATGACTTCTACTCGAACACGAATGCAAAAGCAGAAATGAAATGAATA 2892
_	oy 2555	GCATGGATACCTCAAACAAGAAGAGAAGTTCAGATCTGGTGGAACTGGT
	~	GCATGGATACCTCAAACAAGGAAGAGAAATGAGGATCTCAGGACCTTGGTGGACACTGTG 2952
J	2y 2615	TACACCTCTGCATTCATTGTCTCACAGATGTGACTGTATAACTGTCCAGGTTGGTT
	0b 2953	TACACCICTGGATTCATTGTCTCTCACAGATGTGACTGTALAACTTTCCGAGGTTCTGTT 8012
_	0y 2675	IATGGCCACATTIAATATCITCAGGTCITIIIGTGCALAIAAAATGLGCAGAGGAATTG 2234

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3275 CICAGAALGIAAAAGAACITACIGAITATITICITCAICCAACITATGITITITAAAIGAG 3334 613 CICAGAALGIAAAAAAACITACIGAITAITICITCAICCAACITATGITITIAAAIGAA 5672
23.45 TETGGGTGAFFCCTAAGCCACFFGAAAFGFFAGFCAFFGFFAFFFAFACAAGAFFGAAAA 2794
                                                                                                                                                       4-73 IIIGGGTGATTCCTAAGCCA/IIGAAATGIIAGTCATTGITATTTATAGAAITGAAAA 3132
                                                                                                                                                                                                                                                                              3133 PCTIGIGIAAAFCTIGCAFFFAAAAAGFFGFAGCAGAFFGFFCFFCCFCFFCCAAAGFAAA 3192
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             TCTTCCAAATGCAATTTGATTGACTGCCCATTCACCAAATTATCCTGAAGTCTTGTGCA 3094
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 ** : ICTICCAAAIGCAAIITGAATGACTGCCCATTCACCAAAATTATCCTGAACTTTTGCA 3432
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 3154 AAAAIGGALAITAITAGAAAITAGAAAAAATTACTAATTTTACACAITAGATTTTATTT 3154
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           44 +3 AAAATGGATATTATTAGAAAATTAGAAAAATTACTAATTTTACACATTAGATTTTATTT 3492
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                                                                                                                                                                                                                    2795 TCTTGTGTAAATCCTGCCATTTAAAAGTTGTAGGAGATGTFTCCTCTGTTGCAAAGTAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Human retinoblastoma protein eDNA sequence.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         ABK86079 standard; cDNA: 4740 BP
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22 DEC-2000; 2000KK-0080184.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           3347 GATTATIGATAGT 3347
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ARKBEC73
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bladder, skin, stomach, liver, colon and oral cavity. Tymphoma and leukaemia. The anticancer agent induces apoptotic death of cancer cells and the Rb inhibitor increases the apoptosis inducing activity of rypelation and the profit and another cells. The agent is specific to cancers in which Rb proteins are optionally expressed and mycolactone shows very strong anticancer effect is vited as well as it who.
                                                                                                                                                                                                                                                              Also included for is an anticancer agent comprising mycolactone and antisense inhibitors of retinoblastoma (Rb) protein expression, the anticancer agent is used for the treatment of cancers such as breast,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            HILLIHILIHILIHILIHILIHILI IIIHILIHI II 434 GOGGAATGTGATTIACTGA 493
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   494 GC1ACAGAAAAACATACGAAATCAGTGTCCATAAATTCTTTAACTTACTAAAAGAAATTG 553
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        554 ATACCAGTACCAAGTTGATAATCCTAAGACTGAAGACTGTGAAGAAGTATGTGT 61×
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       614 TTGCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATATTTGACACGCAGCA 673
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                342 -----ATCTACTGAAATAAATTCTGCATTGCTAAAAGTTTCTTGGATCACATTTT 354
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             395 TATTAGCTAAAGGGGAAGTATTAGAAATGGAAGATGATGTGGTTTGATTTGATTAG 454
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    9; Indels 207; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           The invention relates to an anticancer agent comprising mycolactone
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               314 CATTATGTCAGAAATTAAAGATAPTAFATATATATAGAGAGAGAGGTTGGTTAAGTTGGG
                                                                                                                                                                                                                                                                                                                                                                                                                                             The present sequence is the human conA for retinublastoma protein.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     242 AGAAAGTTTCATCTGGATGGAGTATTGGGAGGTTATATATTGAAAAGAAAAGGAACTGI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            93.1%; Score 3114.6; DB 24; Length 4740; 93.9%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Anticancer agent useful for treatment of cuncer e.g. of skin,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Sequence 4740 RP: 1508 A: 887 C; §62 G; 1483 1; 0 other;

*Q2 GGGGAATCTGTATCTTTATTGCAGCAGTTGACCTAGTCGA------
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Pred. No. 0;
0; Mismatches
                                                                                                                                                                                                  Example 4; Page 38-42; 44pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Query Match
Best Local Similarity 93.99
Matches 3337; Conservative
                   (Blog-) BIOGENIA CO LID.
                                                                                                                                                              comprising mycolactone
                                                                                                  WPI; 2002-508397/54.
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FATTAAACTOT FILLEFELLE TATTAAACTOT	ACAGCT	AGCAAAACAACTAGAAAATG FILLIHHHHHHHHHH AGCAAAACAAGAAAATG	GATGAATGTAATATAGATGAGGTGAAAAAT 	LIATGAATTCTFGGAACTTGTAATGGACTTGCAGAGGTGAAAATGTTTGTA 	33ATACGAAGAAATTTAT 	ALGATAAAACTGTTCAGACTGATTCTATAGACAGTTTGAAAGACAGAGAGGAGGAA FELFICHTELLETTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	AAAGTAACCTTGATGAAAAGGGAAAGTAATTCCTCCACATCCCAGTTAGGACTGTTA FEEFFEEFFEEFFEEFFEEFFEEFFEEFFEEFFEEFFE	TGAACACTATCCAACAATTAATGATGATTTAAATTCAGGAAGTGATCAACGTTCAGAAA 	ALCHGALHICCLALTHAACAACHGCACAGTGAATCCAAAAGAAAGTATACHGAAAAGAC FEFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	TGAAGGATATAGATACATCHTAAAGACAAATTIGCTAAAGCTGTGGGACAGGGTTGTG TELLTTTTTTTTTTTTTTTTTTTTTTTTTTT	TOGANATTGGATOACAGGATACAAACTTGGAGTTCGCTTGTATTACCGAGTAATGGAAT 	CCA DCLIAAA LOGAAGAAGAAGA HALCCA LCAAAA FFFTAGGAAACFFCGAAGG FFFFFFFFFFFFFFFFFFFFFFFF	APARATHHEATAHGETHA HIGGEROOGEETTGAGGTTGTAALGGCACATATA TELLHELLHELLHELLHELLHELLHELLHHELLHHELLH	GCAGAAGTACATCTCAGAALCTTGATTGTGGAAACAGATTGTCTTTCCCATGGATTCTGA FELLILLILLILLILLILLILLILLILLILLILLILLILLI	ALGLOCTIAALITAAAAOCOTTIGALTITIACAAAGIGA EGGAAAGITTIALGAAAGCAG TYLLITILITITITITITITITITITITITITITITITIT	ANDOTANCH GALANGANAAN GATAAAATTI AGAAGGATGTGAACALGGAATCATGG TITLITITITITITITITITITITITITITITITI ANGOTANGTI GAGAAAGAAAA GATAAAAAGATGTGAACATGGAATGTGA	AAPOCCTPOCATGOTTCTCA/JATPCACCTTTATTFGATCTTATTAACAATCAAAGGACC 111141111111111111111111111111111111
7.94	5.15 854	5.75 9.14	6.85 974	635 1034	155	н15 1154	875	9.85	1434	1.894	1115	1175	1235	1295	1455	1415	1475
3 G	45 42	70 G	5 CT	55 G2	A 2 2 2 2		5 â		5 £	57 Eb	5 ±	5 g	5 =	25 ± ± ± ± ± ± ± ± ± ± ± ± ± ± ± ± ± ± ±	5 £	7 G	÷ 6

AGAAGCCATTGAAATCLACCCCTCTCTTTGACTGTTTTATAAAAAAGTGTATCGGGTAGCCT 1774 1835 TCATCTGGACCCTTTTCCAGCACACCCTGCAGAATGAGTATGAACTCATGAGAGAAAAAGC 1894 2174 TCATCTGGACCCTTTTCCAGCACACACGCTGCAGAATGAGTATGAACTCATGAGAGACAGGC 2233 1895 ATTTGGACCAAATTATGATGTGTTCGATGTALGGGALALGCAAAGTGAAGALALAGAC 1954 TCAAACGTGTTTTGATCAAAGAAGAGAGTATGATTGTATTATAGTATTGTATAACTGGG 2074 2075 TCTTCATGCAGAGAGTGAAAACAAATATTTTGCAGTATGCTTCCACCAGACACTTAGCT 2134 2414 TOTICATGCAGAGACTGAAAACAAATATTTTGCAGTATGCTTCCACCAGGCCCCTACCT 2473 2375 TCAAAAGAAGTGCTGAAGGAAGCAACCCTCCTAAACCACTGAAAAAACTACGCTTTGATA 2434 2714 TCAAAAGAAGTGCTGAAGGAAGCAAGCCTCCTAAACACTGGAAAAACLACG HTGATA 2773 2255 TGCCAACACCAACAAAAAIGACTCCAAGATCAAGAAATTAGTALCAATTGALGAATCAL 2314 2555 GCATGGATACCTCAAACAAGAAGAAAATGAGGATCTCAGGACCTTGGTGGACACTGTG 2614 2894 GCATGGATACTCAAACAAGGAAGAAATGAGGATCTCAGGACCTTGGTGGACACTGTG 2953 2615 TACACCTCTCGATTCATTCTCTCTCACAGATCTGACTGTATAACTTTCTTACGTTTTTTT 2674 1535 GAGAAGGACCAACTGALCACCTTGAATCTGCTTCTTCTTTAATCTTCCTCTCAAATA 1594 2354 TCAAACGTGTTTTGATCAAAGAAGGAGGTATCATTCTATTATATGTTGTATAACTCGG 2315 TCGGGACTTCTGAGAAGTTCCAGAAATAAATCAGATGGTATGTAACAGGGACCCTGTGC 2435 TTGAAGGATCAGATGAAGCAGATGGAAGTAAAQAFCTGCGAGGGGGGGGTCCAAAFFFGG 1994 CTACGCGTGTAAATTCTACTGCAAATGCAGAAGACAAAGAAGGTCAGCCTTCGACACGC 2234 ATTIGGACCAAATTAIGAIGIICCAIGIATGGCAIAIGCAAAAGGAAATAIAGACC 2135 TGTCACCAATACCTCACATTCCTCGAAGCCCTTACAAGTTTCCTAGTTCACGGA 2195 TICCIGGAGGGAACAICIATAITICACCCCCGAAGAGICCATAIAAAAITICAGAAAGIC 2774 TTGAAGGATCAGATGAAGCAGATGGAAGTAAACATCTCCCAGGAGAGTCCAAATTTCAGC 1955 TTAAATTCAAAATCATTGTAACAGCATACAAGGATCTTCCTCATGTTCTCAGGACAT 2654 PEGGGACIFIC GAGAAGTITČEAGAAA1AAA1CAGA IGGI A I GI TAACAGCOACOLO I GOO 2594 TGCCAACAACAAAAATGACTCCAAGATCAAGAATCTTAGTATCAATTGGTGAATGAT 2015 qq g ŝ ô g ò ć <u>a</u> ŝ qq ŝ g Ś q ŝ qq ò qq ò <u>Q</u> ŝ g ် qq ô q ŝ 5 ŝ 9 ŝ g ŝ d ò

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Meditied retireblastoms tumour suppressor, EISP profeth, canoor Unitapy:
              2954 HACACCITICGALICATTICTOTOTOTOTOTOTOTOTATA ACTITICCCAGGITICTG 3013
                                                         2475 TATGGCCANATITAATATGTTCAGCTCTTTTTGTGGGATATAAAATGTGCAGATGCAATTG 2734
                                                                                                     2735 ITTCCCTCATTCCTAACCCACTTCAAATGTPACTCATTGTTATTATACAAGATTGAAAA 2794
                                                                                                                                                                27.9% ICLIGIGIAAATOOFGCCATTTAAAAAGTTGTAGCAGAFTGTTTCCTCCTTCCAAAGTAAA 2854
                                                                                                                                                                                                                             ATTGCTGTGCTTTATGGATAGTAAAATGGCCTTAGAGTGGGAAATGCTGAFAACCAAGGT 2914
                                                                                                                                                                                                                                                          4194 ALTGOLGI GCITTLATGGAD AGTAAGAA FOGGGOTTAGAGTGCGAAGTGTTAAAGGGAAGGG
                                                                                                                                                                                                                                                                                     3254 CIGTOTGAOTACTTTGCCTTCTTTGTAGGATATAGGTGATGTTTGCTCTTGTTTATTATT 3313
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Modified retinoblastoma tumour suppressor gene.
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protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular
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                                                                                                                                                                                                                                                                                                                              This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                          Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      92.9%; Score 3111; DB 19; Length 3477; 95.9%; Pred. No. 0;
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                                                                                                                                                                                                                                                            inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Mismatches 110;
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                                                                                                                                                        Hu S, Xu II, Zhou Y;
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                                                                                                    (BAYU ) BAYLOR COLLEGE MEDICINE
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                                  98WO-US03041
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27-AUG-1998
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21 40 2221 CGGATTCCTGGAGGGAAVATCTATATTCACCCGTGAGAGTCCATATAAATTTTCAGAA 2280 1801 GCCTATCTCCGGCTAAATACACTTTGTGAAGGCCTTGTGTGAGGAGGCAGAATTAGAA 1860 1831 CAPATCATCICGACCTTTTCCAGCACACACAGAATGAGTATGAAACTCATGAGAAAC 1890 1891 AGGGATTTGGACCAAATTATGATGTTTCCATGTATGGATATGGAAAGTGAAAATATA 1950 1951 GACCTTANATICANANICATIGIAACAGCATACAAGGATCTTCCTCATGTCAGGAG 2010 2101 inderrigardeadadacidaaaacaaaratittideadiatocitoracaacaceeen 2160 2131 ACCITGICACCAALACCICACAIICCTCGAAGCCCIIACAAGIITCCACCTTA 2190 2191 CGGATTCCTGGAGGGAACAFCTATTTCACCCCTGAAAAGTCTATAAAATLTCAGAA 2250 2251 GOTCTGCCAACAACAACAAAAATGACTCCAAGAATCTTAGTATCAATTGGTAA 2310 2281 GCTCTGCCAACAACAAAATGACTCCAAGATGAAAATCITAGTATAATIGGTGAA 2340 2311 TCATTCGGGACTTCTGAGAAGITCCAGAAAIAAATGAGATATGTAACAGCGACCGT 2370 2341 TCATTCGGGACTTCTGAGAAGTTGCAGAAAJAAA FCAGATGGTATGTAAGAGGGGGT 2400 2431 GATATTGAAGGATGAGATGAAGGAGGAGTAAAGATGTGGGGAGAGAGTGTAAAHTT 2490 2641 TGTGTACACCTCTGGATTCATTGTCTCTCAGATGTGACTGTALAACTTTCCCAGGTTC 2700 2701 IGITTATGGCCACATTTAATATCTTCAGCTCTTTTGTGGATATAAAATGTGCAGAGGA 2760 2731 AFFICTITIGGTGATTCCTAAGCCACTTGAAALGTTAGTGATTGFTATTTATAGAAGATTG 2750 1711 ACCAGAAAGCATTGAAATCTACTTCTTTCACTCTTAAAAAAAGGGAACATA 1770 1741 ACCCAGAAGCCALIGAAATCIACCICTCITTICAALIAAAAAAAGTGIAAAGAATA 1800 2011 ACATTCAAACGEGTTTTGATCAAAGAAGAGGAGEATGTATGTATALATALATAAAA 2070 2041 ACATICAAAGGIGITIIGAIGAAAGAAGAGGAGIAIGAIIGIAHIAGIATCITAIAAA 2100 2161 ACCTTGTCACCAATACCTGACATTCCTCGAAGTGGTTACAAGTTTTCCTAGTTTGAGGTTTA 2220 2491 CAGCAGAAACTGGCAGAAATGACITCTACICGAACACGAATGCAAAAGCAGAAAATGAAT 2550 2671 TGTTTATGGCCACATTTAATATCTTCAGCTTTTTGTGGATATAAAATGTGAAGGA 2071 TCGGTGTTGTATGCAGAGTGAAAAAATATTTTGGAGTATGCTTGCACAAAAAT 2551 GATASCATGGATACCTCAAACAAGGAAGAGAATGAGGATCTCAGGACTTGCTGGACAC 2581 GATAGCATGGATACCTCAAACAAGGAAGAAATGAGGATCTCAAGGACCTTGGTGGACAA 2611 TGTGTACACCICTGGATTCATTGTCTCTCAGAGATGTGACTGTAFAACTTTCCAGGTC 2521 CAGCAGAAACTGGCAGAATGACTTCTACTGGAACAGGAATGCAAAAGGAAAATGAAT 2371 GTGCTCAAAAGAAGTGCTGAAGGAAGCAACCTTAAACCACTGAAAAAATTACTTT ò q ŝ 3 ò â Ôγ 3 ô 3 ò g ò q Š g $_{\rm y}$ qq ò 3 ŝ 3 ें 음 òλ 3 ò q ò q ò q ò a a ò d

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22/4] AAAAICIIGIGTAAATCCTGGGATFFTAAAAAGFFGAAATFGFFFGGGGGGGAAG 2850
                             2821 AAAAICTIGIGIGIAAATCCTGCATTTAAAAAGTTGTAGGAAATTGTTGCTGTTCCAAAG 2880
                                                             FAFTAATT FATATGTATATTTTTTTAATTTAACAFGAGGCGTFAGAAAAFGFGFGA 3030
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                                                                                                                                                                       Ibis sequence encodes a modified retinoblastoma tumbur suppressor
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                                                                       Retinoblasions suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                274 GGTTATATTCAAAAAAAAAGGAACTGTGGGGAATCT-------
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                                                                                                                                                                                                                                                                                                                                                                       Pred. No. 0;
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                                                                                                                                  Claim 22; Page 188-192; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                   Local Similarity 94.8%;
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1747 TTTTATAAAAAGIGTALGGGGTAGGGTATCTGCGGTTAAATACACTTTGTGAATGTTT 1806
                                                                               1807 CTGTCTGAGCACCCAGAATTAGAACATATCATCTGGACCTTTTTCCAGCACACGCAG 1866
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                                                                                                                                                                                                                                                                                                                                                                         3127 TACTAATTTTACACATTAGATTTTATTTTACTATTGGAATCTGATATACTGTGTGCCTTGT
Retinoblastoma; cancer, detection, diagnosis, protein, neoplasm;
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comprises comparina genetic material corresponding to a normal
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337..2787
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A method for detecting the presence, in a tumour sample, of a protein the absence of which is associated with a sepplasm, emprises
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                        124 GAGGACCTGCCTCTCTTCACCTTCACTTTTCAAGAAACAAGAAGAAGCTTGATTTTACTGCA 183
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          119 GA-GACCIGCOICOCOPAGOCITGACITICAAGAACAGAAGAACCIGATIIIACIGCA 177
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   358 CTACAGAAAACATAGAAATCAGTGTGTGAAATTGT11AAC11AAG1AAAAGAAATTGA1 417
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                                                                                                                                                                                                                                                                                                                                              3; Indels 210; Gaps
                                                                                                                                                                                                                                                                                                                             244 AAAGITICAICTGEGGAFGGAGTATTGGGAGGTTATATTCAAAAGGAAAAGGAACTGFGG
                                                                                                                        antibody with the tumour sample. Immune complexes indicate the presence of the protein in the sample. The method may be used in the detection and treatment of a defective human gene related to
                                                                                                                                                                                                                                                    DB 15; Length 4597;
                                                                                                          producing an antibody to the protein and then contacting the
                                                                                                                                                                                                                  Sequence 4597 BP; 1489 A; 841 C; 812 G; 1455 T; 0 other;
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human retinoblastoma with DNA from a patient
                                                                                                                                                                                                                                                    92.5%; Score 3096.2;
                                                                                                                                                                                                                                                                                          0; Mismatches
                                                                                                                                                                                                                                                                       Pred. No.
                                Example 2(2), Figure 7; 18pp, English.
                                                                                                                                                                               cancer, in particular retinoblastoma.
                                                                                                                                                                                                                                                                       94.08;
                                                                                                                                                                                                                                                                                        Conservative
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2278 TTCATGCAGAGACTGAAAACAAATATTTTGCAGTATGCTLCCACGAGGCCCCCTAGCTTC 2337 2458 CCAACACAAAAAAGACTCCAAGATCAAGAATTAAGTATCAATTGGTGAATTATTC 2517 2758 ATGGATACCICAAACAAGGAGGAGAGAGGAGGTTCAGGTGGACACGGA 2817 2677 TGGCCACATTTAATATCTLCAGCTCTTTTTTGTGGATATAAAATGTGCAGATGTAALLGTT 2736 1777 CTCCGGCTAAATACACTTTGTGAACGCCTTCTGTGTGAGGGCGCAGAATTAGAACATATC TB36 1897 ITGGACCAAATTATGATGTGTTGCATGTATGGCATATGCAAAGTGAAGAATATAGACCTT 1956 2077 ITCALGCAGACTGAAAACAAAIAIITTGCAGIATGCTTCCACCAGGCCCCTTACCTTG 2136 2137 TCACCAATACCTCACATTCCTCGAAGGCCCTTACAAGTTTCCTAGTTCACCCTTACGGATT 2196 2197 CCTGGGGGGGGGCTCTATATTCGGCCCTGAGGGTCCATATAAAATTTCGCAGTTG 2256 2377 AAAAGAAGTGCTGAAGGAAGCAACCCTCTTAAAQGACTGAAAAAATTACGTTTGATATT 2436 2638 GAAGGATCACATGAAGCAGATGGAAGTAAACATCTCCCAGGAGAGTCCAAATTLCAGCAG 2697 2616 2818 CACCICIOGATIFICATIFICICICICACAGATICI GACTICITATAACTITIFICAGATICI CITITA 2877 2797 ITGTGTAAAICCIGCCATITAAAAAGIIGIAGCAGATIGIIICCICIICCAAAAGIIAAAAI 2856 2398 CCTGGAGGGAACATCTATATTTCACCCTGAAGACTCCATATAAAATTTCAGAAGGTCTG 2457 1957 AAATTCAAAATCATTGTAACAGGATACAAGGATCTTCGTCALGCTGTTCAGGAGACATTC 1717 AAGCCATTGAAATCTACCTCTTTCACTGTTTTATAAAAAAGTGTATGGGCTAGCCTAT 1978 CTCCGGCTAAATACACTTTGTGAACGCCTTCTGTGAGCACCAGAATTAGAACATAC 1837 ATCIGGACCCTTTTCCAGCACACCCTGCAGAATGAGIATGAACTCAIGAGAAAACAT 2038 ATCHGGACCCTTTTCCAGCACCCLGCAGAATGAGTATGAACTCATGAGACACACAT 2098 TTGGACCAAATTATGATGTGTTCCATGTATGCCALATGCAAAGTGAAGAATATAGACTT 2017 AAACGTGTT FEGALCAAAGAAGAGGAGTATGAFTCTATTATAGTAT ICTATAACTFCGGTC 2338 TCACCAATACCTCACTTCTCGAAGCCCTTACAAGTTCCTAGTTCACCTTACAGTT 2257 CCAACACCAACAAAAATGACTCCAAGATCAAGAATCTTAGTATCAATTGGTGAATCATTC 2317 GGGACTTCTGGGAAGTTTCGAGAAATAAATCAGATGGTATGTAACAGGGGCTGTGTCTT 2497 AAACTGGCAGAAATGACTTTTACTGGAACACGAATGCAAAAAGCAGAAAATGAATAATAGC 2557 ATIGGATACCTCAAACAAGGAAGAAGAAATGAGGATCTCAGGAGCTTGGTGGACACTTGTA 2617 CACCICIGGATICATIGICICICACACAGATGIGACIGIATAACITICCCAGGITCTGITIA λō q ò d ò 90 <u>a</u> ò d õ 9 Š q d ò q 9 ò q ô Q : 9 ò q οy 9 ò 2 ò a ò Q (ć ŝ ò ŏ

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3227 GAGAATGTAAAAGAACTTACTGATTATTTTCTTCATCCAACTTATGTTTTTAAATGAGGA 3336
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also makes the human DNA probe pH3-8. Isolated from a human chromosome 13 lambda phage library, was used in a chromosome walk to isolate Rb cDNA, the human DNA probe pH3-8. Isolated from a human chromosome 13 lambda phage library, was used in a chromosome walk to isolate and map 30 kb of genomic UNA surrounding the H3-8 sequence. Fragment pH30.7R (ATCC 97500) was obtained, and was used as a probe to screen a cDNA interprited that had been constructed from an adenovirus 12 transformed human embryonic retinal cell from an adenovirus 12 transformed human embryonic retinal cell retinal class which was not present in 4 retinoblastome and one retinal cells which was not present in 4 retinoblastoma and one osteosaroma cell samples. Ph nucleic acids comprising the kb gene, CDNA or a frayment of the june, such as one of the 27 exons or 26 introns, can be used in a claimed method for detecting a deletion or point mutation in the Rb gene of a human patient. The
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             yene can also be used to synthesize Rb polypeptide (see AAY01542) for use in the treatment of individuals determined to have a detective
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 184 TYAYGYCAGAAATTAAAGATACCAGATÇATGYÇAGAGAGAGCTYGGTYRACYYGGGAG 243
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  244 AAAGTITICATCTCTCTCTCTATTTGGAAACTTATATTCAAAAGAAAAAGAACTGTGG 303
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                                                                                                                                                                            isolated human retinoblastoma gene - used to develop products for amalysing predisposition to retinoblastoma and for the detection and treatment of retinoblastoma
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            3; Indels 210; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  This is the nucleic acid sequence of a cDNA of the normal human retinoblastoma gene Rb. Absence or mutation of the Rb gene (see also AAXO4502) predisposes an individual to retinoblastoma. To
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Match 92.5%; Score 3096.2; DB 20; Length 4597; Local Similarity 94.0%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Sequence 4597 BP; 1489 A; 841 C; 813 G; 1454 F; 0 other;
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(MASS-) MASSACHUSETTS EYE & EAP INFIPMAPY.
                                                                    Yandell DW,
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                                                                                                                                                                                                                                                                      Claim 8; Fig 5; 32pp; English.
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                       (WHED ) WHITEHEAD INST.
                                                                    Dryja TP, Friend S,
                                                                                                               WPI; 1999-094898/08
                                                                                                                                      P-PSDB; AAY01542
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1657 ACCCCTCTAAATTCTACTCCAAATCCACACAACCAACCTTCACCTTCCAGACCAG 1716
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1558 GEGETFAATTTAAAAGGCETFGATTTTTAGAAAGTGGAAAGFFTTTAFGAAAGGAGAA 1617
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24.17 PACCICTG ATTCATTGTCFCTCACAGATGTGACTGTATAACTTTCGCAGGTTCTGTTA 2676
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                                                                             2557 ATGGATACCTCAAACAACAACAACAATGAGAATCTCAGAACCTGGGGGGACACTGTGTA 2616
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Diagnosis of retinoblastoma - using genetic material corresp. to a normal
                                                                                                                                                                                                                                                                                                                                                                                                                                                                         neoplasm. It is used to produce an antibody to the protein, contacting this with the tumour sample and detecting immune complexes as indication of the presence in the tumour sample of the protein. Whose sequence or a unique sub-region can be used. The method identifies patients lacking the defective retinoblastoma (Rb) allele and thus are not at risk of
                                                                                                                                                                                                                                                                                                                                                                                                                                                          This gene encodes a protein, the absence of which is associated with a
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    124 GAGGAGCTIGGGTFGGGTTTTGAGTTTTGAAGAAACAGAAGAACGACTGATTTTTACTGCA 183
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    119 GA-GACCEGOTESTOGICAGOTEGAGAAGAAGAGAGAGAGAGCEGATEFTACTGC 177
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   298 GGAAPCFGFAFFFFFFACAGCAGTTGACTFACATGAGATGFGFFFFFAGTFFFFAGTGAG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    418 ACCASTACCAAASTIGATAAFGCTATGTCAAGACTGTTGAAGAAGTATGATGTATIGTTT 477
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        4; Indels 210; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      92.5%; Score 3094.6; DB 9; Length 4597; 94.0%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Sequence 4597 BP; 1489 A; 839 C; 815 G; 1454 T; U other;
                                                                                                                                                                                                                                                                                                                                                                                            human retinoblastoma gene or a unique sub-region
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    304 GGAATICTGTATCTTTATTTGCAGCAGTTGACCTAGICGA----
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Fred. No. 0;
0; Mismatches
                                              Location/Qualifiers
337..2787
                                                                                                                                                                                                                                                                (WHIT-) WHITEHEAD INST BIOMED RE.
                                                                                                                                                                             87EP-11407095
                                                                                                                                                                                                              86US-0895163
                                                                                                                                                                                                                                                                                                                                                                                                                            Disclosure; ; p; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Best Local Similarity 94.0 Matches 3337; Conservative
                                                                                                                                                                                                                                             (MASS-) MASSACHUSETS EYE
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        developing the disease.
                                                                               /*t.ag-
                                                                                                                                                                                                                                                                                             Dryja TP, Friend S;
                                                                                                                                                                                                                                                                                                                              WPI; 1988-065827/10.
                                                                                                                                                                                                                                                                                                                                          P-PSDB; AAP82112
               Homo sapiens.
                                                                                                                                                                             11-AIR:-1487;
                                                                                                                                                                                                            11-AUG-1986;
                                                                                                                                              09-MAR-1988
                                                                                                              EP259031-A.
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TGACACCACCACT 537 CHECATCACATTITA 396 CHICLILITITITITITI CHICATTACATTATA 597 TTTCATTICATTATA 456 HILLILITITITITITI
AAAAGTTTGTTGGATC AAAAGTTTGTTGGATC TCTGGTGATTTCATTT FLITTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT
GYTAAAGGGAAGTATTACAAATGGAAGATGATGTGGTG
2. TT
478 442 497 598

Cy Dp	1357	GTGCTTAATTTAAAGCCTTTGATTTTTACAAGTGATGGAAAGTTTTATTAAAGGAGGGATGGAAAGTTTTAAAAAGGGTTTGATTTTAAAAGTGATGGAAAGTGATTTTTAAAAAGTGATGGAAAAAGTGAAAAAGTGAAAAAA
o c	1417	GGDAACTTGACAAGAAAAAGATATAAAACATCTAAAACATGTAAAAATGTATAAAAATATAAAAAATATTAAAAAAAA
O O	1477	TCCCTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAAACAACAACGAACCGAACCCTTGCATGGCTCTCAGATTCACCTTATTTAATCTTATTAAACAATCAAAAGGACCGA
oy Ob	1537	GAAGGACCAACTGATCACCTTGAATCTGCTTGTCTCTTAATCTTCTCTCTC
oy ab	1597	597 CACACTGCAGCAGATATGTACTTTCTCCTGTAAAATCTCCAAAGAAAAAAAA
yo da	1657 1858	ACGCGTGTAAATTCTACTGCAATGCAGACACACAACCTCAAGCTTCCAAAACAAAC
ОУ	1717	AAGCCATTGAAATCTACCTCTCTTTCACTGTTTTATAAAAAGGGTATCGGTAGGTTTTTTTT
Q Op	1777	CTCCGGCTAAATACACTTTGTGAACGCCTTCTGTCTGAGCACCCAGAATTAGAACATATC 1836
dy Db	1837 2038	ATCTGGACCCTTTTCCAGCACACCCGGGAGATGAGTATGACTCATGAGACTCATGAGACATTTTGATTTTTTTT
ΟΥ Db	1897 2098	TIGGACCAAATTATGATGTGTTCCATGTATGGCATATGTAAGTGAAGATAAAAAATTATGTTT 1956
Q C	1957 2158	AAATTGAAAATGATGTAAGGGATACAGGGATGTTGGTGATGCTGTTGAGGAAGAGTTG 2016
c cy	2017	AAACGIGITTTGAICAAAAAAGAGGASTAIGATICIAITATAGTAITCIAIAACTCGGEC 2076
oy Db	2077	TICATICAGAGAGACEGAAAAQAATATITIGAGETRACETRACAGAGACACAGAAAAAAAAAAAAAAAAAAAAAAAAAA
Q Q	2137	TCACCATACTCACATTCTCGAAGCCTTACAAGTTCCTAGTCACCTTACGATT 2196 [IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII
o do	2197	CCTGARANAAACATCTATATTTCACCCTGAAGACCATATAAAATTTCAGAGGTCG 2256
QY Db	2257 2458	CCAACACCAACAAAATGACTCCAAGATCAAGAATCTTAATATCAATGATGAATCTTTT 2416 LTTTTTTTTTTTTTTTTTTTTCCAAGATCAAGATCTTAGTATCAATGGTGAATCATTC 2517
Q Q	2317 2518	GGGACTTCTGAGAAGTTCCAGAAAATAAATCAGATGGTATGTAACAGAGACGACGTCTC 2476 [TELETER FELLET FELLET FELLET FELLET FELLET FELLET FELLET FELLET GGGAATCTGGGAAAAAAAAAAAAAAAGGTAATGTAACGGACTGTGGACCTGGGAAACAAAAAAAA
ò qa	2377	AAAAGAAGTGCTGAAGGAAGCAACCTTGTAAAAAAAAAA
^0	2437	GAAGGATCACATGAAGCAGATGGAAGTAAACATCTCCAAGAAGTTCAAATTTCAAGAAGAAGAAAGA

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2758 A FGGATARC FCAAACAAGGAAGAGAATGAGGATCFCAGGACCTTGGTGGACACTGFGTA 2817
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  4217 AGCTGGAAGGAAAGTATAACCATATGATACTATCATACTACTGAAACAGATTTCATACCT 3276
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                                                                                                                                                                                                                                                                                            2818 CACCTCTGGATTCATTGTCTCTCACACATGTGACTGTATAACTTTCCCAGGTTCTGTTTA 2877
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        319 CIATIGGAATCIGAIATACIGIGCIGCIGTITIAIAAAAITITGCITITAAATAAA 3216
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     **** *!TATIGGAATGTGATATACTGTGTGGTTGTTTATAAAAITTTGCTTTTAATTAAATAAA 3417
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                                                                                                                                                      2857 IGCEGEGELEAEGAFAGEAAGAFGGGGGEGGGAGEGGAAGEGGAAGEGAAG
                                                                                                                                                                                Modified retinoblasions tumour suppressor gene
                                                                                                                                                                                                                                                                                                                                                           AAVS#446 standard; DNA; 3323 BP
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protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RTSPs have a broader spectrum of
             Suppressor, ETSP protein; cancer therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              421 AFGGAAGAFGAFGAFGAFTFCATTFCAGFLAAFSCIAFGFGFCCFFGACTAFTTAFF 480
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    61 GAACCCCGGGAAACGCGGCGGAACCCCCCCTCCTGAGGAGGAGGAGAGGAGGAGGACGGCC 120
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 112 -------ATGTCGTTCACTITTACTGAGCIACAGAAAAACATAGAAAICAGTGT 158
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      159 CCATAAATTCTTTAACTTACTAAAAGAAATTGATACCAGTACCAAAGTTGATAALGCTAL 218
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   381 GFATTGGTGCTAAAAGTTTGTTGGATGAGATTTTTATTAGGTAAAAGGGGAAGTATTAGAA 420
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               279 ATGTGAACTTATATATTGACACAAACCAGAGTTCG--ALATCTACTGAAATAAATTCT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      91.6%, Score 3066.2, DH 19; Length 3323;
                                                                                                                                                                                                                                                                                                                                                                                  Retinobiastoma suppressor protein with N-terminal modification inbibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   0; Mismatches 133; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Sequence 3323 HP; 1099 A; 647 C; 588 G; 989 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                           Claim 22; Page 180-184, 249pp, English.
                           cellular proliferation inhibitor, ss.
                                                                                      Location/Qualifiers
                                                                                                                                                                                                                                                              (BAYU ) BAYLOR COLLEGE MEDICINE
          Modified reliachlastoma tumour
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              activity than wild type RTSPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     ilarity 95.3%;
Conservative
                                                                                                                                                                                                      98WO-US03041
                                                                                                                                                                                                                                  9705-0038118
                                                                                                                                                                                                                                                                                                           Χu π,
                                                                                                                                                                                                                                                                               (TEXA ) UNIV TEXAS SYSTEM
                                                                                                                                                                                                                                                                                                         Нu S,
                                                                                                                                                                                                                                                                                                                                       WPI; 1998-480788/41.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Local Similarity
                                                                                                                                                                                                                                                                                                                                                      P-PSDB; AAW69370
                                                                                                                                                                                                                                                                                                         Benedict WF,
                                                          Homo sapiens
                                                                                                                                             WO9837091-A2
                                                                                                                                                                                                      19-FEB-1998;
                                                                                                                                                                                                                                 20-PER-1997;
                                                                                                                                                                           27 - AUG - 1998.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Matches 3190;
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a
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ARGANGALGATETTGTATTEAGTTAATGGTATGTGTGTGTGTGTGTTTTTTTT	GEGAAAALGTI ALTI EGAAAALTTI LAIACCTITTA EGAATTCTCTTGGACTTGTAACA 720 HHIHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	GTAATTCCTCCACACTCCAGTTAGGACTGTTATGAACACTATCCAACAATTAATGATG 960 HITHIHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	CTTGRAGTTCGTTGTATTACCAGATAGGAALGCALGCTTAAATCAGAAGAACGA 1200 HTGLAGGATCGTTGTATTACCGAGTAATGGAATCCATGCTTAAATCAGAAGAAGAACGA 1176 CTTGRAGTTCGTTGTATTACCGAGTAATGGAATCCATGCTTAAATCAGAAGAAGAACGA 1176 HTGLAGGATCATCAAAATTTACCAAACTTCTGAATGACACATTTTTCATAGTCTTTATTG 1260 HTGLAGGATCATCAAAATTTACCAAACTTCTGAATGACACATTTTTCATAGTCTTTATTG 1216 GCGTGCGCTTGAAATTTACCAAACTTCTGAATGACAACATTTTAATGTCTTTATTG 1260 GCGTGCGCTTGAATGAGAAACACACAAAAGAAAAAAAAAA	HITTACAAAGTGATGGAAAGTTTTTATGAAAGGGAAGGGAA
APPGA AAAV16 AAAV16 GITTCA GAAAAA GAAAAAA GAAAAAAAAAAAAAAAAAAA		GTAAT GTAAT GTAAT ATTTZ ACAGIG ACAGIG GAGAAZ GAGAAZ	CTTGG FTTGG FTTGG FTTGG GGGGG GGGGG GGGGG FTTGG FTTGGG FTTGGG FTTTGG FTTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTTGG FTTTGG FTTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTTGG FTTGG FTTTGG FTTGG FTTGG FTTG FTTTGG FTTGG FTTTGG FTTGG FTTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTGG FTTTG FTTTGG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTGG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG FTTTG F	
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q	1477	CCTTTATTIGATCTTATTAAACAATCAAAAGACCGAGAAGGACCAACTGAICACTTGAA 1536
oy :	1561	TCROCTIGECTCTTAALCTICCTCCCAAAAAACACACACACACAAAATTICCAACAAAAAAAA
QC C	1537	TCTGCTTGTCCTCTTAATCTTCCTCTCCAGAATAATCACACTGCAGCAGATATGTATCTT 1596
ò ò	1621	TCTCCTGTAAGATCTCCAAAGAAAAAGGTTCAACTACGGGGGTAAAATTCTACTGCAAAT 1680 HHIIHHHIIHHHIIHHHIIHHHIIHHHIHHHIHHHIHH
δò	1681	GCAGAGACACAAACTCAGCTTCCAGATCCAGAAGCATTGAAATCTACTTTTT 1740
Dp	1657	GERTHER GERTHE
\$ 6	1741	TCACTGTTTTATAAAAAAGTGTATGGGCTAGCTATCTCGGCTAAATACACTTTGTGAA 1800 TCACTGTTTTATAAAAAAAGTGTTTTTTTTTTTATAAAAAAAA
ò	1801	COCCTCTGTGTCTGTGTGTGTGTGTGTGTGTGTGTGTGTG
q	1777	COCCTTCTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT
QY Db	1861	CTGCARAATGAGTATGAAGTGATGAGAGAGGGATTTGGACAAATTATGAAGTGTGG 1920
δÿ	1921	ATGTATGGGATATGCAAAGTGAAGAATTAGACCTTAAATTGAAAATGATTGLAAGAGA 1980
a C	7897	ATGTATGGCATATGCAAAGIGAAGAATATAGACCIIAAAIICAAAALICAIIGIAACAGGA 1956
رج م	1981	TACAAGGAFCTTGCTGATGCTGTTCAGGAGACATTCAAACGTGTTTTGATCAAAGAAGAG 2040 FILLIHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
Οy	2041	GAGTATGATTATTATATATTCTATAGTCGGTCTTCATGAGAGACTGAAAAAAAA
qq	2017	GAGTATGATTGTATAGATTGTATAGATGGTGGTGTTGATGA
ò	2101	ATTTTGCAGTATGCTTCCAGGGGCCCCTACTTGTCACAATACCTCAGATTGCTCAGA 2160
a	2077	ATTITIGGAGIATIGGTT OF ACCAGGGGGGGT ACCELGI CACCAATACH CACAFTGCTGGA 2136
λ α α	2161	AGCCTTACAAATTTACTTACTTACTTACAGATTCTTGGGGGGAACAACATTTATTGA 2220 HILLIHIHIHIHIHIHIHIHIHIHIHIHIHIHIHAAAGAGTAACAACATTATTAGA 2230 AGCCCTTACAAGTTTCCTAGTTCACCCTTACGGATTCCTGAGCGAACATCTATATTTCA 2196
ογ	1222	CCCCCCAAGAGAGATTCAGAAGGTOTGCAAGAGAAAAAAAAAA
Dh	2197	CCCTGAAGAGTCCATATAAAATTTCAGAAGGTCTGCAACAACACAAAAAAGGCTGAACAAAAAAAA
0y 10b	2281	AGATCAGAATCTTAGTATCAATGGTCAATGATTGGGGACTTCTGAGAATTTCAGAAA 2340
δλ	2341	ATANATCAGATGGTATGTAACAGGGACGTGTGCDCAAAAGAAGGAGGTGCTGAAGGAAGDAAC 2400
qq	2317	ATAAATCAGATGGTATGTAACAGGGACCGTGTGGGAAAGAAGTGCTGAAAGGAAGTAGC 2376
oy ob	2401	CCTCCTAAACCACTGAAAAACTAGGCTTTGATATTGAAGGATCAGATGAACAAATGA 2460
Oy Db	2461	461 AGTAAACATGTCCCAGGAGAGTCCAAATTTCAGCAGAAACTGGCAGAAATGACTTCTACT 2520
Š		GGANCACGAATGCAAAAGGAGAAAATGAATGATGATGGATGGAT
qq	2497	CGAACACGAATGCAAAAGCAGAAAATGAATGATAGCATGGATACCTTPAAAGAAGGAAGAAGA 2556
9 0 0 0	2581	AAATGAGGATOTICAGGACCTITGGTGACACTICTIGTACACTICTIGGATTICATTGTTCTCA 2640 LTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT

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2:41 CAGAIGIGACIGIAIAAQIIIGCCAGGIIGIGIIAIGGGCAGAIIIAAIAIGICIICAGCT 2/00
                       2857 AIGAROTANANTGARANTOCTAATAAOOOANAGOOTGIOTAAATATATGATITIGGATIOTITIG 2916
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             2977 AACAIGAAJAGCCIIAGAAAAIGIGIGCIATCIATCITCCAAAAIGCAATTTGACIG 3036
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                                                                                                                                                                                                                                               2/37 ATGTTAGTCATTGTTATATACAAGATTGAAAATCTTGTGTAAAATCCTGCCATTTAAAA 2796
                                                                                                                                                                                                                                                                                                                                                                                                  2881 AIGGCCCIASAGIGGGAGICTGAIAACCCAGGCTGICFACTACFICGCTICIIIIG 2940
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    4061 CCCATTCACCAAAATTAFCCFGAACTCTTCFGCAAAAATGGATATTATTAGAAATTAGAA 3120
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      4241 TGATACTATCATACTACTGAAACAGATTTCATACCTCAGAATGTAAAAGAACTTACTGAT 3300
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                                                                                                                                                                                                                                                                                                                              fibrosarcoma, soft tissue sarcoma, small cell sarcoma,
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                                                                                                                                            The probe can be used to detect tumour with an Rb defect eg
                                                                                                                                                                                                                   Sequence 4579 BP; 1477 A; 843 C; 808 G; 1451 T; 0 other;
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                                                                                                     Claim 14; Page 17; 32pp; English.
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               WPI; 1988-33809/48.
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1974 AACAGCATACAAGGATCTTCCTCATGCTGTTCAGGACATTCAAACGTGTTTTGATCAA 2033 2159 AACASCATACAAGGATCTTCCTCATGCTGTTCATGAGAGACATTCAAAGGTTTTGATAAA 2218 2219 AGAAGAGGAGTATGTATTATAGTGTTCTATAACTCGGTGTTCATCAAGAGACTGAA 2278 2094 AACAAATTITICCAGIALGCITICCAGCCCCCCTAAATTAATAATAAATAAA 2153 2458 GACTCCAAGATCAAGAATCTTAGTATCAATTGGTGAATCATTCGGGACTTCTGAGAAGTT 2517 2454 AGATGGAAGTAAACATGTGGCAGGAGTGCAAATTTFAGFAGAAACTGGGAAAATGGC 2513 2938 ACTIGAAAIGITAGICATIGITATITATACAAGAITGAAAAICITGIGAAAATCGGCA 2997 1794 TIGIGAACGCCTICTGTCTGAGCACCCAGAATTAGAACAIATCATCTGGACCCTTTTCCA 1853 1854 GCACACCCTGCAGAATGAGTATGAACTCATGAGAGACAGGGATTTGGGACCAAATTATGAT 1913 2154 TOCTOGNAMICCETIACAAGIITOGIAGIICACCOTTANAGALIOGIGGAGGAACATOTA 2213 2214 TATTICACCCIGAAGAGICCAIAIAAAA111CAGAAGGICIGCGAACACGAAGAAAT 2273 2274 GACTGCAAGAICAAGAAICTTAGTATGAAIIGGIGAAICATTCGGGACTICTGAGAAGTT 2333 2394 AAGCAACCCTCCTAAACACACTGAAAAAACTACGCTTTGATATGAAGGATCAGATGAAGC 2453 2698 TTCTACTCGAACACGAATGCAAAAGCAGAAALGAATGATAGTAGTAGTTGTTGTAGTAGTAAAAA 2757 2574 GGAAGAAATGAGGATCTCAGGACCTTGGTGGACTGTGTGTACACTCTGGATTCATTG 2633 2758 GGAAGAGAATIGAGGATGTCAGGACCTTGGTGGACTGTGTGTGTGTGTGTTGTTG 2817 2634 TETETEAGAGAIGIGACTGTAIAACHIRECCAGGHEHGHIAAIGGCAACATHAAFAIG 2693 2818 TCTCTCACACACACTGTATAACTTTCCCAGGTTCTGTTTATGCCACATTTAATAIC 2877 2694 IICAGCICTIIIIGIGGAIAIAAAAIGIGCAGAIGCAATIGIIIGGGIGAIHCCTAAGCC 275+ 2754 ACTIGAAAIGITAGICATIGITATITATACAAGATIGAAAAATICTGIGAAAATIGTGOOG 2813 1919 CICICITICACIGITITATAAAAAAGIGTATCGGCTAGCCIATCICCCGGCTAAATACACT 1978 1734 CTCTCTTTCACTGTTTTATAAAAAGIGTATCGGCTAGGTATCTCCGGCTAAATACACT 1793 2039 GCACACCCTGCAGAATGAGTATGAACTCATGAGAGACACATTTGGACCAAATTATGAT 2034 AGANGAGGAGTATGATTGTATTATAGTATTGTATAACTGGGTGTTGTATCATGAACTGAA 2398 TATTTCACCCCTGAAGAGTCCATATAAAATTTCAGAAAGGTCTGCCAACACAAAAAT 2638 AGATGGAAGTAAACATCTCCCAGGAGAGTCCAAATTTCAGCAGAAAACTGGCAGAAAATGAC Š qq င် Q : ŝ q Š qq ŝ 5 ò qq δ qq ŝ å ć g $\overset{\circ}{\circ}$ d ò 9 g ò qq ò 9 ò q ò d ó q ŝ 딥 ô

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2994 (TAATITAACATGAACACCCTFAGAAATGTGTGTATCTATCTTGCAAATGCAALTTGA 3053
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Search completed: January 16, 2003, 23:39:22 Job time: 488.93 secs

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                  Copyright (c) 1994
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numblers search, using frame_plus_pzn model M protein

January 16, 2003, 23:41:58 ; Search time 275,998 Seconds

(Without aliquments) 7011.280 Million cell apdates/sec

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BLOSUM6.2 Scoring table;

Xqapop 10.0 , Xqapext Yqapop 10.0 , Yqapext

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total number of hits satisfying chosen parameters:

2185249 Seqs, 1125999159 residues

Sections

Maximum DB seq length: 2000000000 Minimum DB Seq Tength: 0

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Database :

/Sitiskiztrapiara/quaresiq/gunasiym.combi/Ma1989.DAT;*/Sitiskiztrapiara/quasiyqm.combi/Ma1990.DAT;* CANTEST DATES *: DAT: \$93. DAT: * /stless/graditalspaneseq/genesegn_embl/NAIGHT_DAT++ *-1VI ong (VN/) plue-iibesedeby besedaby by optoby / 2sqls/ /STDSZ/gegelata/genesseg/genessegn-embi/NA1983_DAT: * ** TAU 52 Appropriate Appropriate form of the FMA 1984 in IAT ** *- TACL 28 PLAN LAMO - RESEARCH SERVED TO THE PROPERTY OF THE TACK /SIDS270radata/deneseq/qeneseqn.embl/NA1986.DAT:* /SIDS270radata/deneseq/qeneseqn.embl/NA1987.DAT:* idine inperental administration of SATISS duma-ulassamatylassamatyla pohobylyka pyl Zalbas, a albin, temesen, tessesenso _ubasallab/basallab/r_pptob/zwjjs/ N Genneseq 101002:*

Fred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

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/31bSL/4: qdata/qeneseq/qeneseqn_enbl/NAbs02:DAI:*

/STES: Arrida az regerseg Apenesegn - embl znkla99 .EAT • /STES/Arridata/geneseg/Apenesegn - embl znkla99 .EAT:• /STES/Arridata/deneseg/Apenesegn - embl znk2000 - DAT:•

/Silbsz/gradata/geneseg/genesegn-embl/NA1995.DAT:* 78 (1827) for other a Zironossong Speriossongo (MA) 997 (DAT) * 78 (1882) Syronologia (Zironossong Speriossongo (MA) 997 (DAT) * /S:DS2/deadata/qeneseq/qeneseqn-emb1/NA1944.DAT:*

Result.	Score	Query Match	Query Match Length DB	DB		Description
	4453	100.0	3347	5	AAV58448	Modified retinobla
CI	5	98.86	2994		AA041545	Retinoblastoma gen
×	<u>-</u>	48.8	2994	19	AAV40004	Retinoblastoma pro
4	4401.5	98.8	5094	-;	AAZ40287	Wild type human re-
ഗ	401	98.8	2992	0.7	AAX90450	Human pllo RB reti
Ç.	<u>-</u>	9.86	2645	다	AAH25755	Retinoblastoma tum
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æ	4390.5	9.85	4740	7.7	ABK86079	Human retinoblasto
5	4 186.5	98.5	2995	9	AAOR6 398	Human Rbll@ cDNA.
20	4339	97.4	4597	1.5	AAQ70536	Human retinobla
21	4336	47.4	4597	20	AAX04501	Raman retinoblasto
22	4 1 15	97.4	4:67	<u>,</u>	AAN81469	Human retinoblasto
e e	4240	95.2	3461	5.	AAV58447	Modilied retinobla
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25	4213.5	9.4.6	3455	<u>.</u>	AAV58441	Modified retinebla
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ω (1)	4103.5	2.26	13.55 15.55	<u>.</u>	AAV58442	Modified retinobla
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AL LONMENTS

AAV58448 standard; DNA; 4347 BP. AAV58448

Meditied retinables as that suppressor gene.

02-DEC-1998 (first entry)

AAV58448;

Modified refineblasions tumour suppressor; RISP protein; cancer therapy; certural profiteration inhibitor; ss.

Homo sapiens.

Location/Qualifiers /*tag-

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This sequence encodes a modified retinobiastoma tumour suppressor profety (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 profets. The BISPs can be used for treating diseases characterised by abnormal cellular.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               proliferation, particularly cancers, The KTSPs have a broader spectrum of outivity than wild type RTSPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        8) ValsorgerValAspriyyali endiyciyiyri LeClabyatyshysGulou7rpGly 100
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[2] ValLeuLysValSerTrpIleThrPheLeuLeuAlaLysGlyGluValLeuGlnMetGlu 140

24.AUG-1993 (first entry)

Retinoblastoma gene.

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21 ProAlaProProProProProProGluGluAspFroGluGluAspScrd)yProGlu 40
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    retinoblastoma (RB) protein which may be used as part of a method of controlling cell cycle progression which may be used in combination with therapeutic methods to arrest tumourigenesis in organisms. The
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               for regulating certain physiological processes of the body, such as blood cell produ, and gamete produ. Fragments of the protein are soluble in low concus, of glycerol thus enhancing their value in
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    cell cycle can be reversibly attested in a convenient and safe manner. The protein is used in a compsm. is relatively inexpensive and readily obtainable, and shows little or no toxic effects on
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                healthy cells. It is also compatible with other methods and devices
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               The sequence is that of the retinoblastoma gene which encodes the
                                              RB gene product: p56RB portion; cell cycle progression control;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              retinoblasioma protein or fragment, for use in combination with
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                uses purified
                                                              combination; therapeutic methods; arrest; tumourigenesis; requiation; physiological processes; blood cell product
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 2994 BP; 974 A; 618 C; 594 G; 808 T; 0 other;
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Mismatches:
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                                                                                                                                                           Location/Qualifiers
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/note= "Rb protein"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Disclosure, Fig 9: 68pp; English.
                                                                                                                            Homo sapiens SR-40 cell line.
                                                                                                                                                                                                                                                                                                                                9105-0778510.
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                                                                                                                                                                                       /*tag-
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                                                                                               gamete prodn.; ss.
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* £	ValSerSerValAspGlyValLeuclyclydl 	100	
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43.4	CAGAAAAACATAGAAATCAGTGTGGTATAAAT	10	
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5.1.3	CPCTTCAGGAAATGGAAAGAAGATGTGAAACTTATATATTTGAAATAAGGGAGGAG	678	
11.3 67.3	serThriluIleAsnSerAlaLeuValLeuLysValSerTrpIleThrPheLeuLeu 	131 738	
132	Alatysel - - - - - GCTAAAGG	151 748	•
793	\psi	171 858	
172 859	ThralaValileProileAsnGlySerProArqThrProArqArqGlyGlnAsnArqSer 	191 918	
192 413	<u> </u>	211	
212 174	HISGBUCYSASEBOASEDCUABLISASNVALTYFTRCLISASNFROEDCETTIFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	231 1038	
2.82	٠ - ٩	251	
252 1099	TyrshagtalletyrLouLysAsuLysAspLouAsplaargLeuPheLeuAspliisAsp 	271 1158	
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                                                                                                                                                                                                                                                                              8.42 LeualudluMet Dir Ser Dir Arq Ehr ArqMet GlinLysGlinLysMet AshAspSerMet 851
                                   742 GlydlyAsnileTyrileSerProLeuLySSerProTyrLySileSerGludlyLeuPro 751
                                                                                                                                                                               7.2 ArqSerAladludlySerAsuProProLysProLeuLysLysLeuArqPheAspIleGlu
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bladder cancer; restenosis; andioplasty; diabetic retinopathy;
thyroid hyperplasia; Grave's disease; pseriasis;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                New Lusion polypeptide of, e.g. transcription factor—Tuse
treat, e.g. hyper proliferative disease such as cancer and
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Peripheral vascular disease; therapy; ss.
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protein RB (See AAWACASS). A new claimed polypeptide is a lusion of the autraction actor (TP) comprising a both binding domain, and (ii) a transcription lactor (TP) comprising a both binding domain, and (ii) a retinoblastoma (Rb) polypeptide that includes a growth suppression domain. Also new are: (I) a nucleic acid curoding the suppression protein, and (2) expression vectors containing such bna. The tusion protein, particularly expressed from gene therapy vectors (especially admoviture vertors), is used to treat hyperproliferative conditions, specifically cancer (particularly of the bladder) or restenosis (after angioplasty), but also diabetic retinopathy, thyroid hyperplasia, drave's discose, psoriasis, benign prostatic hypertrophy. In Fraumeni syndrome and portible at a provided. The fusion proteins are more effective in repressing transcription of the EEF promoter than Rb alone and cause cell-cycle transcription of the EEF promoter than Rb alone and cause cell-cycle
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               81 ValSerSerValAspGlyValLeuGlyClyTyrlleClnLystysEysCluLeufrpGly 100
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                                       This nucleotide sequence includes a coding region for retinoblastoma
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        61 CysClaigsLeulysTleProAspHisValArgGluArgAlaTrpLeuThrlipGluLys
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Example 1; Fig 2A; 91pp; English.
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                                                             532 ThralaAlaAspMetTyrLeuSerProValArgSerProLysLysLysSlyserThrThr
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2899 GATACCICAAACAAGGAAGAAA 2922

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RR quier human; retinolastome gene; mutation detection; immunoscreening; rethoshastoma datamass i hereditary rethoshastoma; secondary cancer; ostresarroma; diloblastoma; breast cancer; throsarroma; diloblastoma; breast cancer; throsarroma; diloblastoma; breast cancer;
                                                                                                                                                                                                                                                                                                     (wterting relimoblastoma gene cancer in mammals -
                                                                      Wild type human retinoblastoma qene.
                 AAZ40287 Standard; cDNA; 2994 BP
                                                                                                                                                                                                                                                                                                                      Example 6: Fig 7: 34pp; English.
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                                                    24 FEB 2000 (first entry)
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                                                                                                                                     Botto sapiens.
                                                                                                                                                                                          07 JUN 1995;
                                                                                                                                                                                                            15 OCT 1987;
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                                                                                                                                                       US5998144 A.
                                                                                                                                                                        or DEC 1999.
                                   AA240287;
RESTEL 4
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This sequence represents the wild type human retinoblastome quie. The invention relates to a method of defecting a mutated retinoblastoma (mRE) nucleic acid in mammals comprising hybridizing an isolated defecting the limit length, wildstype RE (wREB) cDNA probe to a cell sample and detecting a mutated RE nucleic acid. The method is useful as a diagnostic tool for diagnosing retinoblastoma. RE CDNA or genomic DNA are preferably used as probes to determine the defect region of the mRE gene through genomic DNA blotting analysis of using the method of restriction fragment length polymorphism analysis to determine the diseased illele. Cloped FR screening and for the prediction of the development of secondary cancer, such as, osteosarcoma, tibrosarcoma, qlioblastoma, breast, cancer whether or not connected with retinoblastoma. The method is also used in the suppression of tomorisewise where the absent RB protein ppHHIIO will be provided through the molecular induction and gene transplanting of the RB cDNA to the individual in need of ppRBIIO. antibodies which are useful for immunoscreening of tissue blopsy. The diagnostic method is particularly intended for use in screening families with a history of hereditary retinoblastoma and for screening CDNA can be used to generate specific anti RB protein (anti-ppRB110) their children. It may also be used in prophylactic and postnatal

Sequence 2994 BP: 974 A: 518 C: 594 G: 808 T: 0 other;

A. I. HILLING SCHOOL CS.			
Pred, No.:	3	Length:	2994
Seaugh et al.	4401.50	Matches:	8.28
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δ	232	AshSerLeuGlyLeaValThrSerAshGlyLeuProGluValGluAshLeuSerLysArq 251
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                                                692 MetGlnArgieutysThrAsnileLeuGlnIyrAlaSerThrArgProProThrLeuSer
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Human; pil0-RB; retinoblastoma; tumour suppressor; gene therapy; adenoviral protein IX, recombinant adenovirus explossion vector; cell cycle, p53, mitosio, cell death, apoptosis; thymidine kinase;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Human pl10-RB retinoblastoma tumour suppressor encoding cDNA.
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/note- "retinoblastoma tumour suppressor"
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25-00T-1993;
19 MAY 1994;
28-00T-1997;
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The present invention describes a composition comprising a recombinant adenovirus expression vertor, where the vector has an insert of exoperious DNA comprising a quie encoding a foreign protein and adenovirus DNA in which all of the coding sequences of Ela, Elb, and protein IX, and part of El are deleted, the vectors are useful in gene therapy treatment of cancer, especially for treating p53 delicient unions. The vector enables safer and more ettlicient gene therapy of cancer. The present sequence encodes human p110 KB retinoblastoms tument suppressor which can be used as the foreign gene in the above Recombinant adenoviral vectors asetal for gene therapy of cancer, N. S. I.I.W. especially p53 deficient tumours aselosure; Fig 3: 50pp; English Maneyai D', 1999 443568/37 C'ANU DEPARTE INC P. PSDB: AAY24471 dregery RJ, =**x**366**x**b=**x**3**x**366666666666

Sequence 2995 BP; 975 A; 618 C; 593 G; 809 T; 0 ottler;

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The present invention describes an adenoviral expression vector comprising a delation in the protein IX gene and a gene encoding a foreign protein. This vector can be used in your therapy, particularly to introduce tumour suppressor genes into cancerous cells, Genes which may be used include p53, thymidine kinase and intimublational temour suppressor gene (Rb). The present sequence is the retinoblastoma tumour
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Percumbinant adenovirus expression vector comprising a partial or total deletion of a protein IX DNA and a gene encoding a toreign protein e.g. suicide protein, useful for inhibiting or reducing the proliferation of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Retinoblastoma; tumour suppressor profein; Rb; p53; cancer; adenoviral vector; gene therapy; thymidine xipace; do.
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45 G	47.4	HisclucysachileaspoluvaliysashvaliyrFhelysashPhoileFroPheMet Hillillillillillillillillillillillillill	38
ŝ	7 4 7	AsnSer Lend) ylenVal ThrSerAsnGlyLenProGluValGluAsnLenSerLysAra	
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	7.1.7	[xx fhr tend lathrAspSer [leAspSer Pleck] affect hazaThr ProAnd veSer 29	
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~.	74.7	AsnicuAspiludiuVa.iAsniva.iTietrofroHis.iArproVa.iArqifirVd.MetAsn.317	1.1
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Db	1339	FILEFILLE HELLE HE	1 1.98
cy.	352	AspileClyfyr HethetyschutysthaAlatysAlaVateTychotycysVateTu	171
ΟÞ	1399	GATATAGGATACATCTTAAAGAGAAATTTGCTAAAGCTGTGGAACACAGGLLGTGTGGA	1458
δ :	372	372 IleGlySerchnArqTyrLysLeuGlyValAraLesTyrArgValMetGluSerMet (9)	1.4.1
<u>a</u> 3	454 202	AFFIGATEATCACAATACAAACTTIGAACTTIGAATTACAATGAATGAATGAATGAATGAATG	= :
à d	1519	LOTEMATORANGA MANDEL THE THE THE THE THE THE THE THE THE THE	411 1578
Oy	412	HethettsMetSerleuLeuAlaCysAlaLeuGluValValMetAlaThrTyrSerArg	4 5.1
qq	1579	ATTITION TANGEST AND A STATE OF A	16 48
ć	432	SerThrSerGlnAsnLeuAspSerGlyThrAspLeuSerPheProTrp11eLeuAsnVal	4 5 1
qq	1649	AGTACATCTCAGAATCTTCATTCTGGAACAGATTTGTCTTTCCCATGGATTCTGAATGTG	1698
0.5	-7F	ZeuAsuZeubysAlaPheAspEheTytbysVilleShaserihettetysAladiothy	17
qq	1699	CTIAATITAAAAGCTTTGATTTTACAAAGTGATCGAAAGTTTTATCAAAGCASAAGG	1758
ΟŸ	472	Asniceuthr Argel aMet Hetyshis Lendinar gryschaff sargiteMet Gluser	1.4
qq	1759	AACTTGACAAGAAATGATAAAACATTTAGAACGATGTGAACATCGAATCATGGAATGC	1818
ζ	492	LeuAlaTrpLeuSerAspSerProLeuPheAspLeu1]eLysGlnSerLysAspArgGlu	511
Q C	1819	CTTGCALGOCICTCAGATICACCTTTATTTGALCTTALIAAAGAATCAAAAAAAAAAAAAA	1878
9.	512	GlyProThrAspHisLeaGlaSerAlaCysProLeaAsmLeaFroLeaGlaAsuAsaHis	1,41
qq	1879	GGACCAACHGATCACCTTGAATCTGCTTTTAATCTTCTTCTCTCTCTCT	1948
ςò	532	ThrataAlaAspMcTlyrLeuSerProValAtqSerProLystysClyserThrThr	155
qq	1939	ACTGCAGGAGTATGTATGTTCTCTCGTAAGATGTCCGAAAGAAA	1498
ολ	. 552	ArgValAsnSerThrAlaAsnAlaGluThrGlnAlaThrSerAlaPheGlnThrGlnLys	571
пр	1999	CGTGTAAAFICTACTIGCAAATIGCAGAGACACAAGGAAGCTCAGCCTTCCAGACCAGA	2058
ΟŅ	572	ProLeuLysSerThrSerLeuSerLeuPheTyrLysLysValTyrArdLeuAlaTyrLeu	591
qq	2059	CCATTGAAATCTACCTCTTTCACTGTTTATAAAAAAGTGTATGAGCTAGCT	2118
ολ	592	ArgleuAsnThrleuCysGluArgleuLeuSerGluHisProGluLeuGluHis Heffe	6.1
QQ	2119	COGCIAAATACACTITGIGAACGCCTTCTGTCTGAGCACCAGAATTAGAACATATCATC	2178
ογ	612	TrpThrLeuPheGlnHisThrLeuGlnAsnGluTyrGluLeuMetArqAspArqHisLeu	6 1 1
90	2179	TGGACCTTTTCCAGCACCCTGCAGAALGAGTALGAGTCATGATGAGAGAGGATTTTT	223B
Οy	632	AspClntleMetMetCysSerMetTyrClytLeCystysValLysAailTeAspLenLys	159
QQ	2239	GACCAAATTATGATGTGTTCCATGTATGGCATATGCAAAGTGAAGTATATATA	86,77
ογ	652	Phetys Het levalthr Ata FyrtysAsplauProHisAlaValGlndlutha Phatys	17.9
Op	2299	TECANANICATION TO THE TACARGE TO THE TECHNICAL STATEMENT OF THE TECHNICAL S	2 45.8
ςò	672	ArqValleufleLysGluGluGluTyrAspserflefleValltheTyrAsnserValPhe	6.41
00	2359	CGTG PTPTGATCAAAGAAGAGGAGTATGATTGTATTATAGTATTCTATAACTCGGTCTTC	2418
o _y	692	Met GInArqLeuLysThrAsn11eLeuGlnTyrAlaSerThrArqProFroTh1LeuSer 	711

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deticablastomas NR summar suppressor protein; pllOpR; p53; gene therapy; excession; authorized an ipsecialic adenoviral protein IX; psociasis; thyroid hyperplasia, drawe's disease, hepatocellular carcinoma; neoplasm; benefit postatic hypertrophy; 11-Frammeni syndrome; sixtle cell anagemia; layesets disease; lewesemia; layesets adenovirus vector; cancer; ss.
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241.4 ATGCAGAGACTGAAAAGAAATTHTGCAGTATGCTTCCACCAGGCCCCCTAGCTTGTCA 2478
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             MIL GlySerAspoluAlaAspolySerLysHisLeuProGlyGluSerLysPheGlnGlnLys 831
                                                                                                                                                                                                                                                                                                                                                                752 ThrProThcLysMe*ThrPreArgSerArgIleLeuValSerIleGlyGlySerPheGly 771
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       842 LeaAlaGluMetThrSerThrArqThrArqMetGlnLysGlnLysMetAsnAspSerMet 851
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p110RB"
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               AADP4474 Standard; cDNA; 2995 BP.
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PPESCH: AAEO0689.
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New recombinant adenovirus expression vector having a gene encoding for a fortigh profession at partial or foral deletion of the absorptial profesion IX but assettled in gene therapy for treating or reducing hyperprolliferative cells.

Disclosure, Fig 3, 49pp; English.

protein, designated as pl10RB.
The investion relaises in a reception of the adequated protein characterised by the partial or total deletion of the adequated protein ix PNA beginning at mucleorides 357 or 360 and ending at 4°20-4050, and for screening tumour suppressor genes useful in gene therapy. The vertor is particularly useful for treducing hyperproliferative cell disorders such as thyroid hyperplana. Grave's disoase, psoriasis, benign prostatic hypertrophy, if Frankeni syndrome, vancets specifically hepatoceilular cardinoma, neoplasms, lumphomas, cre, to inhibit tumour proliferation or to ameliorate particular related pathology such as sickle cell anaemia and Tay-Sachs disease. The vertor The present oDNA sequence encodes retinoblastoma (RB) tumour suppressor useful for the safe recombinant production of diagnostic and reed having a gene encoding a foreign protein such as tumour suppressor protein, pl10RB (retinoblastoma) and p53. Adenovirus vector is used therapeutic polypeptides and proteins.

Sequence 2995 RP; 975 A; 618 C; 593 G; 809 T; 0 other;

Alignment Scores:			
Pred. No.:	0	Length:	2995
Score:	4401.50	Matches:	828
Fercent Similarity.	92.468	Conservative:	0
Best Lonal Similarity.	42.468	Mismatches:	-
Query Match:	98.84%	Indels:	69
DB:	22	Gaps:	1

US-09-026-459A-43 (1-859) x AAD04474 (1-2995)

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470-6	-025-4748-4 (1-879) * AAD044/4 (1-2995)	
	MctProbrogysThrProAnglySThrAlaAlathrAlaAlaAlaAlaAlaAlaAlaAlaCo	
3.50	ATGEORGE AAAAA COO GAAAAAAAAAA GAAGAAAAAAAAAAAAA	
2.1	ProAlaProProProProProProGluGluAspProGluGlnAspSerGlyProGlu 40	
(T	PROTECTION OF THE PROPERTY OF	
4.1	AspLeuProLeuValArgLeuGluPheGluGluThrGluGluProAspPheThrAlaLeu 60	
259	GACTICLITITITITITITITITITITITITITITITITITI	
61	CysClm.ysl.co.ysl.deProAspHisValAr4Cl.Ar4AlairpicuilhrirpClnhys 80	
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ام	ValSorSerValAspClyvalLeuGlyClyTyTlleGlaLySLySLySChnLeuTypCly 100	
379		
101	-	
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112	11.2	
499	CAGAAAAAAAATAGAAATGAGTGTGCATAAATTGTTTAAGTTAGTAAAAGAAATTGATAGG 558	
112		
559	AGTACCAAAGTTGATAATGCTATGTCAAGACTGTTGAAGAAGTATGATGTTTGTT	
112	11.7	
<u>6</u>	CTCTTCAGGAAATTGGAAAGGACATGTGAACTTATATATTTGACAAAACCCAGAATTGG 678	

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	4 4=5	CysValtawAsptyrPbefletysteuSerProProMetteuta 	Thrataval HegrolleasiidlySerproargThrProargArgClySthasiiargSer 	AlaArgTi-AlaLysQlube-ChuAsuAspThrArgTi-Cli-GluValLe-uCysLysGlu +	HESCHRÖSSASH D-ASPSTRADALDSSASRATITTEPEDSSASRBHETTEPEDPEDPPED HELLER HELLER HELLER HELLER FELLER HELLER HELLER HELLER HELLER HELLER HELLER FELLER AND SASARANA SASANA AND HELLER HELLER AND SASARANA SASARANA MARKANA	ASIDSCTICOCTYLOUGHTH FILE THE	Pyrolischalle Fyrbeidyskontyskapteerkapalaargizeibbeteekaphliska Etti etti etti etti etti etti etti etti	Lysthi Lewilithi AspsertteAspserPheGluThrGladrgThrProdrqLysser 	A - A S D - C - C - C - C - C - C - C - C - C -	ThrileGinginLeuMetMetileCeuAsnSerAlaSerAspGinProSerGiuAsnLeu 	These TyrebeardasecysThrvalasterolysoluserTheteutysargvallys HTHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	ASPTH-CLFTPT TO Photy SCHILYS PhoAlary SALAVALGLYGINGLY PYSVALGLU HILLIH	The styse of nary proystend by alarquer pyrtyrargyalmetoluse met.	Doutysseerlluchuchuarqfouserthochasaphasaerlysteuteuasanaspasa 		Ser Broserd Lasside (Asposent) y Thraspide (Ser PheProTrip1) et en asn Vallette (Anna 1907) e	LeubsoleettysklabbekspbhetyrtysValtleGtuserbhetleLysklaGluGl 	<
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1999 CGTGTAAATTUMACTIGCAAATIGCAGAGAGAAGGAAAGTIGAGGGTTYXGAGAGAGAAG 2058
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        2539 GGAGGGAACATATTTCACCCCTGAAGAGICCAIATAAAATTICAGAAGGICLGCCA 2598
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   2599 ACACCAACAAAAATGACTCCAAGATCAAGAATCTTAGTATGAATTGGTGAATCATTCGGG 2658
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                                                                                                                                                                                                                                                                                                                                                                                                                                                     632 AspOln HeMetMetCysSerMetTyrClyfleCystysValtysAsbHteAsphaniys 651
                            492 LeuAlaTrpLeuSerAspSerProLeuPheAspLeuIleLysGluSerLysAspArqGlu 511
                                                                                                                                                                                                                                                                                                                                 592 ArgleuAsnihrleuCyschuArgleuLeuserChuHisProchuLeuChuHishleile 611
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      692 MetGinArgleulysThrAsnileLeuGinTyrAlaSerThrArgProProfhiLeuSer 711
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          752 ThrProThrLysMetThrProArdSerArd11eLeuValSerTleGly31uSerPhed1y 771
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                                                                                       512 OlyproThrAspHisLeaGluSerAlaCysProLeuAsula uProLeuGluAshAshHis
                                                                                                                                                532 ThralaAlaAspMotTyrLouSorProValAraSorProLystysLysClySorThrth
                                                                                                                                                                                                          552 ArqValAsnSerThrAlaAsnAlaGluThrGlnAlaThrSerAlaPheGlnThrGlnLys
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Per includatomia, tument suppressor protofu, pil0 88, cell cycle, p53. Recombination of death, adonoviral profein IX; gene therapy eyostatic, advanceins expression vector; tumensmall cell lung cancer; small cell lung cancer; sealt cell lung cancer; hepatocarcinoma; hepatocellular carcinoma;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            motanoma, retinoblastoma, colorectal carcinoma, sarcoma, Wilm's tumour, dstromytoma, qiloblastoma, neuroblastoma, ovarian carcinoma,
/product- "retinoblastoma tumour suppressor protein"
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Median was retinoblastoma, breast fumeur, colorectal carcinoma, sarcoma, presture tumour, bladder tumour, tumour of the reticuloendothelial tissues, Wilm's tumour, astrocytoma, glichlastoma, neuroblastoma, ovarian carcinoma, osteosarcoma or renal cancer. The present sequence encodes the retinoblastoma tumour suppressor protein pile-RR, which is

given in the exemplification of the present invention. Sequence 295 BP; 975 A; 618 C; 593 G; 809 T; 0 other;

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979 CATGAATGTAATATAGATGAGGTGAAAALGTTTATTTGAAAAATTTTTATACCTTLLATG TU3B
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Modified relinoblastoma tumour suppressor; KTSP protein; cancer therapy; cellular proliferation inhibitor; ss.
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612 TrpThrLeuPheGlnHisThrLeuGlnAsuGluTyrGluLeuMetArqAspArqHisLeu 641
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 profess (RISP) of the invention. The proteins can be used for inhibiting cellular profileration when condministered with a p^{\rm rat} protein. The PISPs can be used for treating diseases characterised by abnormal cellular.
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Matches:
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113 · SerThrGluileAsnSerAlaLeuValLeuLysValSerTrpHeThrPheLeuLeu
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tetracycline responsive expression vector (IREV), which contains a sequence enroding a fusion protein comprising a transcriptional transactively on domain (TTD) generalizely attached to a tetracy line repressor protein (TRP), the lirst sequence operatively positioned downstream of a promoter. The vector also contains a cloning site operatively positioned downstream of a basal promoter comprising a tetracycline operator, the TREVS can be used to produce stable cell lines in which gence expression is rightly regulated by tetracycline. They can be used for the production of proteins such as tumour suppression profession is the production of proteins such as tumour suppression profession to the production of proteins such as tumour suppression.
The present sequence appears in the specification, which describes
                                                                                                                                                                                                                                                                                       Minimal promoter; tetracycline responsive expression vector; TREV;
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                                                                                                                                                                                                                                                                                                          transcriptional transactivation domain; TTD;
tetracycline repressor protein; TRP; tetracycline operator;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      by abnormal cellular proliteration, particularly cancers.
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tumour suppressor protein; treatment; cancer; ss.
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treat conditions related to (premature) ageing, e.g. macular degeneration
                                                                                                                                                                                                                                                                              The invention concerns methods and readents for extending the life span, e.g. the number of mitotic divisions, of a cell. The method relies on activation of a telomerase activity and inhibition of one or hoth of a retinoblastoma (Rb)/INR4 pathway or a p5% puthway. Phospbarylation of Rb by cyclin-dependent kinases, coke and coke, releases the cells into the by cyclin-dependent kinases, coke and coke, releases the cells into the suppressor pleinka, inhibits kinase activity and results in another suppressor pleinka, inhibits kinase activity and results in another arrest. Rb inactivators can selectively and reversiby inactivate an Bb/INK4 pathway, especially an Br/pleinK4 pathway. The enceptotels MDM2 is cellular inhibitor of RB/EEF function and the p5% tumout suppressor and can also be used in the methods, other molecules which can be used include cdk4 or cdk6 mutants. In particular, a cdk4 mutant is one which satisfiers from at one or more constants.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    and arteriosclerosis. The cells can also be used to replace tumour cell. Times in vitro and for studies on licellemical and physiological aspects of growth and differentiation. Long lived (immortal) cells could also be of use in the production of normal or genetically enquered.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Additional constructs include a papilloma virus E7 protein, or other viral ecopy of the will harpasses Bb and/or ff. Antisense constructs of the Rb and plbinK4a genes may also be used. The methods are useful for increasing the profiferative capacity of cells, the cells are subsequently of use in pharmaceutical and cosmette proparations used to
                                                                          New method for increasing the proliferative capacity of cell lines comprises administering agents reversibly activating telemerase activity and recepibly inactivating ELTARA usifor per pathways useful
                                                                                                                                                                                                                            Claim 5; Page 121-123; 123pp; English.
                                                                                                                                                                    in treating age related diseases
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Sequence 4839 BP; 1534 A; 902 C; 880 G; 1524 T; 0 other;

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tabilitate the development of spreening assays to evaluate the potential
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              interaction of androgen receptors and androgen responsive elements to modulate androgenic activity. The identification and characterisation of androgen receptor to activators such as those of the invention will
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Novel androgen receptor associated proteins used to detect androgenic
                                                                  812 GLYSCTASPULDATaAspCLYSCTLySHISLCUPTOGLYGLUSCTLySPhcGlnGlnLys 841
                                                                                                                                                                                                                                                                                                                                                                                                                                              Human; androgen receptor coactivator; ARA54; ARA55; ARA24; detection;
                                                                                                                                                                                                                                                                                                                                                                                                                                                           Rb; androquit; antiandrogenit; identification; prostate cancer; ss.
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                                                                                                                                                                                                                                                                                                                                                                                                            Human androgen receptor coactivator Rb encoding cDNA SEQ ID No-7
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            or antiandrogenic activity in screening assays for candidate pharmaceutical molecules which promote or inhibit the activity
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Human; cancer; colon, breast; ovary; ocsophagus; kidney; thyroid;
stomach; lung; prostate; pancreas, carcinoma; antitumour, cancerous;
cytostatic; gene therapy; antineoplastic; Wilm's tumour; adenocarcinoma;
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(AVAL.) AVALON PHARM.

Young PE, Augustus M, Carter KC, Ebner R, Endress G, Horrigan S; Wedver Z; Sopport DR,

WPI: 2002-188264/24.

Screening for anti neoplastic agent involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, and determining a change in expression of a gene of a signature gene set.

Claim 1: SEQ ID 1210; 44pp: English.

The present invention describes a method (MI) for screening for an anti-neoplastic agent. The method invelves expessing cells to a chemical activity determining a change in expression of at least one gave (I) of a signature gave set, where (I) expression of at least one gave (I) of a signature gave set, where (I) comprises a sequence (S) selected from 8447 sequences (given in ABL61664 to ABL70110), or is at least of anti-neoplastic activity. (B) has cytostatic cypression is indicative and can be used for producting a product which at an anti-neoplastic activity and can be used for product which is the data collected with respect to the anti-neoplastic agent as a result of ML, and the data is sufficient, to convey the chemical results of structure and/or properties of the agent. MI can be used in the treatment of cancer such as solon, breast, stomach, lung, thyroid, orsophatical ovarian, kidney, prostate or parereatic cancer, orsophatical cancer, infiltrating ductal cancer, infiltrating ductal cancer, infiltrating ductal cancer, infiltrating ductal cancer, infiltrating lobular cancer, squamous call carcinoma, neuroendocrine

	XX SQ Aliqui	Seque	nce 4839 BP; 1534 A; 902 Scores:	C) 880 G; 1524 T; 0 other;	
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	λο d	132	AlaLysGlyGluValLeuGlnMetG	AlaLysGlyGluValLeuGlnMetGluAspAspLeuValTleSerPheGlnLeuMetLe	z — .
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	ολ	<u>⊸</u>	AlaArqlleAlaLysClnLeuGluA		7.1
	qq		GCACGGATAGCAAACAACTAGAAA	ATGATACAAGAATTATTGAAGTTGTCT	GTAAAGAA 977
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X E	27 ADG 19	1998.
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X ± 3	20 FEB 19	1997; 970S 0048118.
223	(BAYU) B (TEXA) U	HAVLOR COLLEGE MEDICINE. UNIV TEXAS SYSTEM.
×	Benediet	WP, Hu S, Xo H, Zhon Y;
žžž	WPI; 1998 4807882 P PSDB; AAW69376.	МРТ: 1998 4Н0788741. P. PSDB; AAM69376.
×II	Retinobla unhibitin	Meditoblastoma suppressor protein with Neterminal modification - unbibiling colubation profited for particularly career
× 23	Claim 22;	Poge 226-230; 240pp; English.
* 888888	This sequential (cellular can be us prolifera activity)	This sequence encodes a modified retinoblastoma tumour suppressor protein (RISP) of the invention. The proteins can be used for inhibiting cellular proliteration, when coadministered with a p54 protein. The RISPs can be used for treating diseases characterised by abnormal cellular proliteration, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
X	Sednotto	Sequence 3554 BP: 1170 A; 683 C; 653 G; 1048 F; 0 other;
Fred. Score: Fercen Hest L OB:	Arthundor Scores: Secret Secret Forcent Similarity: Hest Local Similarity March: March:	1
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5 3	1 Met P 	MetbroprougsThreroargigsThralaalafhralaalaalaalaalaalaalaabo 20
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2647 GGATCAGATGAAGCAGAAGTAAACAICTCCCASGAGAGICCAAAITTCAGAGAA 2706
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Location/Qualifiers
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andemia, fay-Sach's disease, ss.
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Best Local Similarity:
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832 LeuAlaGluMetThrSerThrArgThrArgMetGln1ysGln1ysMetAshAspSerMet 851
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Recombinant, adenovirus, expression vector, 180; small lung cancer: hepatecearginems; melanoma, retinoblastoma, sarchau, sickle cell;
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qq	1219 AACCI	FIGATGAAGAGGTGAATGCTTCCTCCACTCCAGTTAGGACTGTTATGAAC	1278
οy	312 Thril	eGInGInLeuMetMetHelleudAsnSerAlaSerAspGInProSerGluAsnLeu	3.11
00	1279 ACTAT		1 4 48
Ś	332 Ilesc	orTyrPheAsnAsnCysThrValAsnFroLysGluSerIleLeatysArqValLys	151
qc	1339 ATTTC	SCIALITITAACAACTGCACAGTGAATCCAAAAGAAAGTATGGAAAAGAAGTGAAG	7.7
Oy	352 Asp11		171
qq ·	1399 GATAT	IAGGATACATCTTTAAAGAGAAATTTGCTAAAGCTGTGGGGACAGGGTTGTGTCGAA	1458
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Oy	432 SerT	ITSerGInAsnLeuAspSerGIyIhtAspLeuSerPheProTrpf LeteuAsnVal	451
â .	1639 AGTAC	SATCTCAGAATCTTGATTCTGGAACAGATTTGTCTTTGCCATGGATTCTGAATGTG	1698
δ	452 LeuAs	80LeuLysAlaPheAspPheTyrLysValIleGluSerPheIleLysAlaGluG]y	471
q Q	1699 CTTA	ATETTAAAAGCCETTEGATTTTTTTACAAAGTGGATGGAAGTTTTTTA FCAAAGCAGAAGGC	1758
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65	512 GlyPr	COTHEASPHISE-BUGLUSGEAL aCysProfeuAsnLeuProfeuGluAsnAsnHis	531
qo	1879 GGACC	SAACTGATTELLE TO THE TOTAL TOTAL TOTAL TOTAL TOTAL SAACTAGATAATTAATTAATTAATTAATTAATTAATTAATT	84.5
Οy	532 ThrAl	laAlaAspMetTyrLeuSerProVajArqSerProlysLysGlySerThrThr	551
Dp	1939 ACTGC	AGCAGATATGTATTTTTTTTTTTTTTTTTTTTTTTTTTT	1998
ΟŸ	552 ArgVa	al Asuser thr Ala Asua la Gluthr Cin Alathr Ser Alathrachaide in 1975	571
a	1999 CGTCT	FAATTETTAGTGCAAATGCAGAGACAGAACGTCGTCTTTTTTTTTT	2058
ò	572 ProLe	auLysSerThrSerLeuSerLeuPhcTyrLysLysValTyrArqLyuAlaTyrLeu	591
qo	2059 CCATT	IGAAATCTACTCTTTTTTTTTTTTTTTTTTTTTTTTTTTT	2118
Οy	592 Argue	vuAsn'tht LeuCysGluArgleulz-uSerGluHisProGlufz-uGluHis Helle	6.1.1
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qq	2239 GACCA	AAATTATGATGTGTTGCATGTATGCAAAGTGAAGAAGAAATATAGTTTAAA	3677
ΟŸ	652 photy		6.71
qq	2299 TICAN	NATCATTGTAACAGCATACAA8GATCTTCCTCATGCTGTTCAGGAGACATTCAAA	834.8

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2559 ACTECTORGAGATTCCAGAAAATAAATCAGATGGTAACGTAACGACGGGCCGTGTGCTCAAA 2718
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572 AraValtaulleLysGluGluGluTyrAspSerIleIleValPheTyrAsnSerValPhe 691
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			Description		Modified retinobla	Modified retinobla	DNA sequence of th	Human retinoblasto	Human androgen rec	Breast cancer rela	Human retinoblasto	Human retinoblasto	Human retinoblasto
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                                                                                                                                                                                                                                                                                                                                                           this sequence encodes a modified retinoblastoma tumour suppressor protein (RISP) of the invention. The proteins can be used for inhibiting recibilar proliferation, when coadministered with a p53 protein. The BTSPs cut be used for treating diseases characterised by abnormal cellular polifieration, particularly cannors. The BTSPs have a breader spectrum of
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                                                                                                                                          Retinoblastoma suppressor protein with N-terminal modification
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astoma fumbour suppressor; RTSP profein; cancer therapy; ation inhibitor; ss.
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                         LTATGGATAGTAAGAATGGCCCTAGAGTGGTAGTCTGGATAACCCAGG 3120
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S SYSTEM.
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This sequence encodes a modified retinoblastoma tomour suppressor proteins can be used for inhibiting conidar polification, when conductisted with a p53 protein. The RISPs can be used for treation, when conductisted by a broader of lular prolliferation, particularly cancers. The RISPs have a broader specific prolliferation,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             12) CCGGARTAPOPTGCCTCTCTCAGGCTTGAGTTTGAGAAGAGAAGCTGATTTTAGT 180
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                                                                                                                     inhibiting cellular proliferation, particularly cancer
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2941 GTTTGGGTGATTGGTAAGGAGTTGAAALGTIAGTATGTTATTATATAAAA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           +1 TOGGDATCTGTATGTTATTGCAGTGACCTAGGTGATATGTCGTTCACTTTACT 360
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       the present sequence appears in the specification, which describes a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     terracycline responsive expression vector (TREV), which contains a sequence encoding a tusion protein comprising a transcriptional
                                                                                                                                                                                                                                                                                             Most forthogonal to most asset of posters and for the tightly controlled expression of genes, such as tumour suppressor
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                       841 AAAGAACATGAATGTAATATATAGATGATGAAAAATGIITATITCAAAAATTTTATATACCT 900
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601 TIATTAGCTAAAGGGGAAGTATTACAAAISGAAGAIGAIGIGGIGAIIICAIIICAGIIA 663
                                                                                               661 ATGCIAIGIGICCIIGACIAIITIAIIAAACICICAAAGIGIGGAAGIGGIGGAAAGAACCA 728
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AEST2; telomerase; catalytic sabunit, reverse transcriptase, life span;
retinoblastoma; p53; tumour suppressor; inhibitor; arterioselerosis;
proliferation; immortal; tumour therapy; macular degeleration; activator;
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                                                          AAA29391 standard; DNA; 4839 HP
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Theat conditions related to (premature) agents, e.g. machiat determination and attentosclerosis. The cells can also be used to replace tumour cell these in vitro and for studies on biochemical and physicological aspects of growth and differentiation. Long lived (immortal) cells could also be of use in the production of normal or genetically engineered.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         e.g. the number of mitotic divisions, of a cell. The method relies on antivarion of a telemerase activity and inhibition of one or both of a retinoblastom of Rb Junka pathway or a p53 pathway. Phosphorylation of Rb by cyclin dependent kinases, c&q and cd&b, releases the cells into the division cycle. Binding of INK4 tamily members, e.g. the tumour suppressor pleTNR4a, inhibits kinase activity and results in quowth division cycle binding of Environmental and results in quowth the test. While interivators can selectively and reversibly inactivate an ELCINY is a cellular inhibitor of Rb/ICET function and the p53 tumour suppressor.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       the invention concerns methods and reagents for extending the lite span,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Additional constructs include a papilloma virus P2 protein, or other viral oncoprotein which bypasses Rb and/or p53. Antisense constructs of the Rb and plenukka genes may also be used. The methods are useful for increasing the proliferative capacity of cells. The rells are is beequeptly of use in pharmaceutical and cosmettic preparations used to theat conditions related to (premature) against e.g. maralar degeneration
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             and can also be used in the methods. Other molecules which can be used include cdk4 or cdk6 mutants. In particular, a cdk4 mutant is one which differs from at one or more if residues K22, R24, H95 and/or P97.
                                                                                                                                                                                                                                                                                                                                                                                        o mprises administering agents reversibly activating telemerace activity and reversibly hazefung Ph/INK4 and/or p3 pathways useful
                                                                                                                                                                                                                                                                                                                                                                   Now method for increasing the proliferative capacity of cell lines
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      laim 5; Page 121-123; 123pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                           in treating age related diseases
                                                                                                                                            98US-0109891.
                                                                                              99WO-US27907
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                                                                                                                                                                                                                    (GENE-) GENETICA INC.
                                                                                                                                                                                                                                                                    Harmon GJ, Heach DH;
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W-200041238-A2.
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122 POGAGGACCTGCTCTCGTCAGGCTTGAGTTTTGAAGAACAGAAGAGCTGATTTTACTG 181

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1273 IGAACACTATCCAACAATTAATGATTTTAAATICAGCAAGTGATCAACCTTCAGAAA 133 973 AAGAACATGAATGTAATATAGATGAGGTGAAAAATGITTATTTCAAAAATTTTATATACCTT 1032 962 AACGATACGAAGAAATTTATCTTAAAAATAAAGATCIAGAIGCAAGATTATTTTGGATC 1021 1082 AAAGTAACCTTGATGAAGAGGTGAATGTAATTCCTCCACACACTCCAGTTAGGACTGTTA 1141 1213 AAAGTAAGGTTGAJGAAGAGGTGAATGCTGCTGCACACTGCAGTTAGGAGTGTTA 1272 1333 ATCTGATTTCCTATTTTAACAACTGCACAGTGAATCCAAAAGGAAAGTATACTGAAAAAGGG 1392 1262 TGAAGGAIAIAGGATACAICITIAAAGAGAAAITIGGIAAAGCIGGGGCAGGGITGIG 1321 1322 TOGANATIGGARCAGEGAIACAAACIIGGAGIICGCIIGIATIACCGAGIANIGGAAI 1381 1382 CCATGCTTAAATCAGAAGAAGAAGGATTATCCATTCAAAATTTTAGCAAACTTGTGAATG 1441 433 GGGGAATFTGTATCTITATTGGAGGAGIIGACCIAGAIGAGAIGTCGTTCACTITTACTC 452 362 AGCTACAGAAAAACATAGAAATCAGTGTGCATAAATTGTTTAACTTAGTAAAAATTG 421 542 GTICGATAICIACTGAAATAAAITCIGGATIGGIGGTAAAAAGITTGTIGGATGACATITT 561 79% DGCIATGIGICCTGACIATITATIAAACICTCACCTCCCAIGITGCTCAAAAAAAGAL 852 782 GGAGIGCACGGAIAGCAAAACAAQIAGAAAIGAIACAAGAAITAFTGAAGIFCTCIGIA 841 302 GGGGAATGTGTAHGTTTATTGGAGGAGTTGAGGTGATATGTGTGGTTGAGTGTTAGTG 361 493 AGCTACACAAAAACATAGAAATCAGTGCCATAAAFTSTITTAACTTACTAAAAAAAAATTG 552 482 TIGCACICTICAGGAAATIGGAAAGGACAIGTGAACIIATATTIIGGACAAAAGGACA 541 602 TATTAGCTAAAGGGGAAGTATTACAAATGGAAGATGTATCTGGTGATTTCAGTTAA 661 733 TATTAGCTAAAGGGGAAGTATTACAAATGGAAGATGATGGTGATCTGGTGATTTCAGTTAA 792 722 ATAAAACAGCIGTIATAACCATTAATGGTTCAGCTCGAACACCCAGGCGAGGTCAGAACA 781 662 JOGTATGTGTGT-JGAGTATTTAAAAGTGTGAGCFGGGATGTFGTGAAGAAGGAT 902 ITATGAATICICITGGACIIGIAACAICIAAIGGACIICCAGAGGIIGAAAAICITICIA 1093 AACGATACGAAGAAATTTATCTTAAAAATAAAGATCTAGATGGAAGATTATTTTGGATC 1022 ATGATAAAACTCTTCAGACTGTTTCTATAGACAGTTTTGAAACACAGGGAACACACAGAA 1153 AIGATAAAACTCTTCAGACTGAITCIAIAGAAGIIIIGAAACACAGAGACACCAGGAA 1142 TGAACACTATCCAACAATTAATGATGATTTTAAATTCAGCAAGTGATCAACCTTCAGAAA 1453 ICGAAAIIGGAIGACAGGGAIAFAAAGIIGGAGIICGCIIGIAIIACCGAGIAAIGGAAI q(i ; <u>۾</u> ò 셤 Ö qq qq ò

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독음	2442	4.0	
4 3	2402	TROUGGAGGGAACHCHAINTHEACGCEIGAAGAGICCAFATAAAATHCAGAAGGFC 2461 FEFFER GAGGGAACATCHAINTHEACGCEIGAAGAGICCATATAAAATHCAGAAGGFC 2592	
7.5	246.2	IGCAACAACAAAAAABSACIGGAAGAICAAAGAAICITTAGIAICAAIIGGIGAAICAT 2521	

2881 2941 1061 171 1 + 1(:] 2893 GCATGGATACTCAAACAAGAAAAAAAAAAAAATCTCAGAGAAYYTTGGTGGAAAACGTG 2952 2593 TGCCAACAAAAAAAAAAGACTCCAAGALCAAGAATCTTAGLATCAATGATGATGAATCAT 2652 2713 TCAAAAGAAGTGCTGAAGGAAGCAACCCTCCTAAACCACTGAAAAAACTACGCTTTGATA 2772 2762 GCATGGATACCFCAAACAAGAAGAAGAATGTCAGGACTTCAGGACTTGGTGTCTTGTG 2821 3013 TATGGCCACATITAATA1CIICAGCICIIIIFGIGGA1A1AAAALGIGCAGATGAATIG 3072 ± ∃ ∃ 2833 AGAAACTGGCAGAAATGAVTTCTACTCGAAVAGAATGVAAAAGYAGAAAAGGAATGATA 3122 CIGICIGACTTICCITTTGCATTTGTAGAATALAGGIGAIGTTGTTGTTTATT 3482 CICAGAATGTAAAAGAACTTACTGAFTATTTCTTCTTCAACTTALGTTTTTTTAAATGAG 2702 AGAAACTGGCAGAAATGACLIGTACTGGAACACGAAATGCAAAAGGAAAAATGAAATA 2822 TACACCTCTGGATTCATTGTCTCTCAGAGATGTGACTGTATAACTTTFCCCAGGTFCTGTT 2882 TATGGCCACATITAATATCTTCAGCTCTTTTTCTGCATAFAAAATGTCTGTAALGTAATTG 2653 TCGGGGCTTCTGAGAAGTTCCAGAAAATCAGATGGTATGTAAGAGGCGTGGG 2642 TIGAAGGAICAGATGAAGAGAGAAGTAAAGATGTGGGAGGAGAGTGGAAATTTGAG 2953 TACACCIC IGGAITCATTGICICICACACACIGICACIATAANTI LOOMAGGI LOOMA 2942 ITTEGGETGATTECTAAGGPACTTGAAATGTTAGTFGTTGTTTGTATGTAAAAA 3002 TCTTGTGTAAATCCTGCCATTTAAAAAGTTGTAGCAGATTGTTTCCTTCTTCCAAAGTAAA 3062 ATTGCTGTGTTTATGGATAGTAAGAATGGCCCTAGAGTGGGGAGTCCTGATAACCAAGC 3253 CTGTCTGACTACTTGCCTTTTTGTAGAATATAGGTGATGTTTGATCTTGTTTATT 3182 AATITATATATATITITITAATITAACATGAACACOCITAGAAAATGIGTOOTAFOTA 3242 TOTTCCAAATGCAATIIGALTGACTGCCCATTCACCAAAATTATCCTGAACTCTGCA 3362 TACTATTGGAATCTGATATACTGTGTTGTTTTTATAAAATTTTGCTTTTAAATA 3422 AAAGCIGGAAGCAAAGIATAACCAIAIGAIACIAICAIACIACIGAAACAGAITICAIAC 3673 GATTATIGATAGI 3685 3542 GATTATTGATAGT 3554 역 --ŝ qq ŝ ŝ **a** ŝ <u>a</u> $\stackrel{\sim}{\circ}$ d ŝ q ô G ò 음 ò 9 ô q ô â ŝ 3 ŝ a ò qq ò 3 ò a ें qq ć

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fact: tate the development of screening assays to evaluate the potential efficacy of drugs in the treatment of prostate cancer.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      the present sequence encodes a human androgen receptor coactivator destinated 8b. Androgen receptor exactivator proteins from the present invention can be used in screening assays to identify candidate pharmaceutical molecules for the ability to promote or inhibit the interaction of androgen receptors and androgen responsive elements to modelate analogues activity. The identification and characterisation of androgen responsive elements to addition receptor co-activity. The identification and characterisation of androgen receptor co-activity and above of the invention will
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Move' androgen receptor associated proteins used to detect androgenic or antiandrogenic activity in screening assays for candidate pharmaceutical molecules which promote or inhibit the activity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Human andrigon receptor positivator, APA54, APA55, APA24, dofertion, No. ention, No. androgenic; antiandrogenic; identification; prostate cancer; ss.
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                                        AAZ88444 Standard; cDNA; 4839 BP.
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1153 AFGATAAAACTCTTCAGACTGATTCTAFAGACAGTTTTGAAACACAGAGAAAACACGAGGAA 1212
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                                                313 CATTATGTGAGAATTAAAGAFAGGAGAIGIGAGAGAGAGAGAIGGIIGGIIAAGIIGGG 372
                                                                                              373 AGAAAGITICAICIGGAIGGAGIAIIGGGAGGIIAIAIAITCAAAAGAAAAAAAACGAACIGI 4+2
                                                                                                                                                                                             302 GGGGAATGTGTATGTTTATTGCASCAGTTGAGGTAGGTATGTGATGTTGCTTCACTTTTACTG 361
                                                                                                                                                                                                                     482 TEGGACTOTTOAGCAAAFEGGAAAGGAGAEGTGAACTTATAFAFFEGAGAGAGGGAGA 541
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              602 FAFTAGCTAAAGGGGAAGTATTAGAAATGGAAGATGATGAGTGAFTTGATFFCAGITAA 661
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362 ASCIACASAAAAAAAIAAAAAICASIGICCAIAAAIICIIIAACITACIAAAASAAAIIG 421
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                                2402 ITCCIGGAGGAACAICTAFAITICACCCTGAAGAGICTAIAIAAAAIHCAGAAGGIC 2461
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                                                                        2533 TTCCTGGAGGAACATCTATATTTCACCCCTGAAGAGTCCATATAAAATTTCACAAGGT
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                                                                                                                                               2593 TGCCAACAACAAAAATGACTCCAAGAATCTTAGTATCAATTGGTGAATCAT
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Human, cancer: colon; broast; ovary, desoplaqua, kidney, thyroid; elements from process; carrinoma; antimour: cancerius; cyroctatio; ane therapy; antincoplastic Wilm's timour, adequations.
         34.8.2 FIGARAA REFRAAAAAAAAATIPACTGAFFTITTITTITIFOATOOAACIIDAUGIFTITIIAAAATGAG 3541
                                                                                                                                                            Breast cancer related gene sequence SEQ 1D NO:1210.
                                                                                                     AHLA2873 standard; DNA; 4839 HP.
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20000S-235720P.
20000S-235720P.
20000S-235840F.
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2000US-236034P.
2000US-236109P.
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2000US-234923P,
2000US-234924P,
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2000US 237294P.
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2000US-234503F.
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2000US-235677F.
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                                    3542 GALLALFGATAGT 3554
                                                      34.73 GATTALLIGATAGT 3685
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28 SEP-2000; 2
24 SEP-2000; 2
24 SEP-2000; 2
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SEP-2000;
SEP-2000;
SEP-2000;
SEP-2000;
                                                                                                                                                                                                                             Homo sapiens
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SEP-2000;
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                                                                                                                       ABL62873;
                                                                                          ARLF 2414
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The present invention describes a method (M1) for screening for an animal and incoplastic agent. The method involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, determining a change in expression of at least one gene (1) of a signature gene set, where (1) comprises a sequence (s) selected from 8447 sequences (given in ABL51664 p. 1-ART9110). At 12 at 12 at 12 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 at 13 
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              adenocarcinoma, carcinoma, clear cell cancer, infiltrating ductal cancer,
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                                                                                                                                                                            Carter KC, Ebner R, Endress G, Horrigan S:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            253 CHRARGARCTGCGCGTCAGGCTTGAGTTGAAGAACAGAAGAACCCTGATTITACTG 312
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                                                                                                                                                                                                                                                                                                                                                                                          chemical agent to be tested for anti-neoplastic activity, and determining a change in expression of a gene of a signature gene set
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                infiltrating lobular cancer, squamous cell carcinoma, neuroendoctine carcinoma, papillary carcinoma and Wilm's tumour.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               193 AAGCCGGGGAPANANANANANGCTCTGAASAASAANAAAAAAAAAAAAA
                                                                                                                                                                                                                                                                                                                                                        Screening for anti-neoplastic agent involves exposing cells to a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     99.9%; Score 3549.8; DB 24; Length 4839; 99.9%; Pred. Mo. 0; 49.9%; Pred. Mo. 0; Mismatches 2; Indels 0; (
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Claim 1; SEG ID 1210; 44pp; English.
01-NCV-2000; 2000US-244867P.
01-NCV-2000; 2000US 245084P.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Best Local Similarity 99.9
Matches 2551; Conservative
                                                                                                                                                                                Augustus M,
                                                                                                                                                                                                                 Weaver Z;
                                                                                                        (AVAL-) AVALON PHARM.
                                                                                                                                                                                                                                                                                     WPI; 2602-188264/24.
                                                                                                                                                                                                                 Soppet DR,
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A method for detecting the presence, in a tumour sample, of a protein the absence of which is associated with a necplasm, comprises producing an antibody to the protein and then contexting the antibody with the tumour sample. Immune complexes indicate the presence of the protein in the sample. The method may be used in the detection and treatment of a defective human gene related to
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Matches 3545; Conservative
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7457 1864 1.75 7104 24.2 TCCCTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTAAACAATCAAAGAACAA 1743 2284 TTCATGCAGAGAGAGAAACAAATATTTGCAGTATGCTTCCACAGGCCCCCTAGCTTG 2444 2584 AAAAGAAGTGCTGAAGGAAGCAACCCTCCTAAAACACTGAAAAAAATAACGTTTGATATT 2643 1498 AGAAGTACATCTCAGAATCTTGATTCTGGAACATTGTCTTTTCCTATGGATT 1GAAT 1557 1564 GTGCTTAATTTAAAAGCCTITGATTTTTACAAAGTGATCGAAAGTTTTATCAAAGGAAAGAA 1924 AAGCCATTGAAATCTACCTCTCTTTCACTGIIIIAIAAAAAAGIGIALGGGCTAGCTAT 1983 1618 GGCAACT FGACAAGAAAATGATAAAAACATTTAGAACGATGTGAACATCGAATCATGGAA 1738 GAAGGACCAACTGATCACCTGAATCTGTCTCTTAATCTTCTCTCACACAATAAT | 1804 | CACACIGGAGCAGAAAGTATOTTOTTOTAGAAGAICTOTAAAGAAAAAAAGATTOAACT 1798 CACACTGCAGCAGATATGTATCTTTCTCCTGTAAGATCTCCCAAAGAAAAAAGGTTCAAACT 1864 ACCCUIGIAAAIICIACIGCAAAIGCAGAAAACAAGCAACCITCAGCCTFCCAGACCAG 1984 CHCCGGCFAAATACACFFFFGFGAACGCFFFCFGFGFGAGCACCGAGAATTAGAAAFAFF 2104 TTGGACCAAATTATGATGTGTTCCATGTATGGCATATGCAAAGTGAAGAATATAGACTT 2098 TTGGACCAAATTATGATGTTCCATGTATGCATATGCAAAGTGAAGATATAGAACT 2164 AAATICAAAAFGATIGIAACAIACAAAGGAIGITGCICA HAMIGITGA SAGATACI 2158 AAATTOAAAATCAITGIAACAGCAIACAAAGAICITGCICATGTTGAGGAGAAAATTC 2344 TCACCAATACCFCACALLCCFCGAAGCCCTTACAAGTFFCFTACTTCACCTLLACGAATT 23.48 TCACCAATACCTCACATTCCTCGAAGCCCTTACAAGTLTCCTAGTLCACCCTAACTAACAATT 2464 CCAACACCAACAAAAATGACTCCAAAGATCAAGAATCTTAGTATCAALTGGTTGAALCATTC 1624 GGCAACTTGACAAGAGAAATGATAAAAGATLTAGAANGATGTGAACATCGAATGAAGAA 2044 ATCTGGACCCTTTCCCAGCACACCCTGGCAGAATGAGTATGAACTCATGAGAGACAA 2224 AAACGIGITIIGAICAAAGAAGAAGAGIAITAICAIITAIAAGIATIGIAIAAGIG 2404 CCTGGAGGGAACATCTATATTTCACCCCTGAAGAGI CCATATAAAATTTCAGAAGGTCTG 1684 2284 ζŎ. ŝ qq qq ŝ â G 9 ò qq q ŝ 3 ŝ Q Q õ â ć 3 ó ç 3 Пþ 3 ŝ ŏ 93 3 ć ें ŝ Ś

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                                                                                                           2754 ATGGATAPPTCAAACAAGGAAAAAAAATAAGGATMTMAGGAAMTGGGAAMTGTA 2823
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                                                                                            Notinoblastoma, Rb gene, human, predisposition, diagnosis, therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            This is the nucleic acid sequence of a cDNA of the normal human retineblasticma gene Rb. Absence or mutation of the Rb gene (see also AAX04502) predisposes an individual to retinoblasticma. To isolate Rb cDNA, the human DNA probe pH3 8. isolated from a human chromosome 13 lambda phage library, was used in a chromosome waik to isolate and map 30 kb of genemic PNA surrounding the HP38 sequence. Pragment pPNA (ALCC 97500) was obtained, and was used as a probe to screen a cDNA library that had been constructed
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            gene can also be used to synthusize Nb polypeptide (see AAN01542) f
use in the treatment of individuals determined to have a defective
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            trom an adenovirus 12-transformed human embryonic retinal cell
line. This provided clone p4 7k ARC (9788), which in Northern
blots cross-reacted with a 4.7 kb transcript in transformed
retinal cells which was not present in 4 retinoblastoma and one
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        99.0%; Score 3520.2; DB 20; Length 4597; 99.8%; Pred. No. 0;
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                                  Human retinoblastoma gene cDNA.
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Best Local Similarity
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                                                                                                                                                                                                  Homo sapiens.
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                                                                        1324 GAAATTGGATCACAGGGATACAAACTTGGAGTICGCTIGIALIACCGAGIAATGGAATCC 1483
                                                                                                                                                                                                                                                                                                                                                                   1318 GAAATTGGATCACAGGATACAAAC11GGAGTTCGCTIGTATTACCGAGTAATGAAICC 1377
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                                                                                                                                   2.444 TCACCAATACCTCACATTCCTCGAAGCCCTTACAAGTTTCCTAGTTTCACCCTTACGGATT 2403
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Diagnosis of retinoblastoma · using genetic material corresp. to a normal human retinoblastoma gene or a unique sub-region
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   neoplasm. It is used to produce an antibody to the protein, contacting this with the tumour sample and detecting immune complexes as indication of the presence in the tumour sample of the protein. Whole sequence or a unique sub testion can be assed. The method identifies patients lacking the defective retinoblastoms (Rb) allele and thus are not at risk of
                                                                                  This gene encodes a protein, the absence of which is associated with a
                                            3424 AGCTGGAAGCAAAGTAIAAGCATATGAIACTAICAIACIAACIGAAACAGAITICAIAGYI 5483
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0, Mismatches
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                                                                                                                                                                                                                                                                                                                              Human retinoblastoma gene.
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                                                                                                                                                                       3538 TTATTGATAGT 3548
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<u>a</u>	1148	AACACTATCCAACAATTAATGATGATTTTAAATTGAGGAAGTGATCAACTTTCAGAAAATTT	197
D C	1204	CTGATTECTATTTTAACAACTGCACAGGAALCCAAAAGAAAGTALACLGAAAAAAGG L. [25.3
οy	1264	AAGGATATAGGATACATY LITAAAGAGAAATT LGCTAAAGCTGTGGGACAGGGTTGTGTGT	¥23
QD	1258	ANGGATATAGGATACATCTITAAAGAGAAATTGGTAAAACTGTGGGAACAGAGGTGTGTCT	117
6 6 7	1324	324 GAAATTGGATCACAGGATACAAACTTGGAGTTGGCTGTALIACCGAGTAATGGAATCC 188 	1 48 4
Qy Db	1384	ATGCTTAAATCAGAAGAAGAAGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGAC HELLILLI HELLILLI HELLILLI HELLILLI HELLILLI HELLILLI HELLI ATGCTTAAATCAGAAGAAGAAGGATTATCCAJ FCAAATTTI AGCAACTTCTAAALGACT	44 4
Ģλ	1444	AACATETTCALATORY LI AT 1836STORO C'ITOARST 191AA 1838YACALATARY T	503
qq	1438	AACATTTTGATATGTCTTTATTGGCGTGCTCTTGAGGTGTAATGGCCACATATAGGT 14	497
λ 2 2 2	1504 1498	AGAAGTACATCTCAGAAATCTTGATACTGGGAA AGALLIGEELLICECA BGATETGGAAT LE 	5.6.3
ò 5	1564 1558	GTGCTTAATTTAAAAGCCTTTGATTTTACAAAGTGATCGAAAGTTTTATCAAAGAAAAAAAA	624
ò	1624	GCCAACTIGAAAAAGAAAAAAAAAAAAAAAAAAAAAAAAA	
qq	1618		677
Çy Db	1684 1678	TOCCTIGCATGGCTCTCAGATTCACCTTTATTGATCTTATTAAACAATCAAAGGGCCGA 15 	743
άō	1744	GAAGGAACTAACTGACACTIGAALCTGGTGTGTGCTCTTAAFCTTCGTGTGTGAATAAT 18 	803
G 0	1804	GAAAGGCCAACTGCACTTGAATCTGCTTGTCCTCTTAATCTTCTCTCTC	797
q _O	1798	CACACTGCAGAGATATSTATCTTCTCTGTAAGATCTCCAAAGAAAAAAAGTTTTTTTT	857
90 20	1864	ACCCTGTAAATTCTACTSCAAATGCAGAGACACAAGCTCAGCTTCAGCTTCAGACTTCTAGATTTTTTTT	1924
à i	1924	ARSCATTGAAATCTACTCTCTTTCACTGTTTTAJAAAAAGTGTAJCGGCJAGCTAT 19	9.B. 4
<u> </u>	13.18	AMBOCATTGAMATCI MOCTOTOT TTCACTGTT TATAANAAMGTGTATCGGTTAGTCTATT	477
<u> </u>	1978	CHOOGE JAMEN ALTHOUGH OF THE STATE MAGE ACCORDED TO THE STATE OF COORDINATE OF THE STATE OF THE OF THE STATE	2 2
ογ	2044	ATCTGGACCCTTTTCCACACACACCCTCACAATGAGTATGAACTCATAAAAAAAA	10.4
QC.	2038	ATCTGGACCCTTTCCAGTACACCTGCAGATGAGTATGAATTCATGAGAGAGA	7603
40	2104	TTGGACCAAATTAIGAIGTGTTCCATGTATGCATATGCAAAATGAAAGAATATAGCTT 23 HTH HTH HTH HTH HTH HTH HTH HTH HTH HTH	116.4
Oy Db	2164 2158	AAATTCAAAATCATGTAACAGCATACAAGGATCTIPCTECATGCTGTTCAGGAGACATEC 2. 	223
5.	* 0000	AAACGICITITGAAAGAAGAAGAAGTATGATTTATAGITTGITGITGITGITGITGITGITGITGITGITGITGIT	7 H Z
<u>1</u>	2218	AAACCHCTT TTCA ICAAACAACAACAACAACAACAAACAAAAAAAAAA	523

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2.28 TICALGGGAGAGAAGAAAAAAAAAATTTTGGAGATTGCAGGGCCCCTACCTTG 2337
2284 HIPALGYAGAGACTGAAAAGAAATALITTGGAGTATGCATTGCAGGGCCCCCTACCTTG 2343
                                                                                                                                                                                                                                                                                                                                          2 / 14 | CARCAALACCICACATICCICGAAGCCCTTACAAGTTTCCTAGTTCACCCTTACGGATT | 2403
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Also included for is an anticaneor agent comprising mycolartone and antisense inhibitors of retinoblastoma (Rb) protein expression. The anticancer agent is used for the treatment of cancers such as breast, bladder, skin, stomach, liver, colos and oral cartty, lymphoma and loukacmia. The anticancer agent induces apoptotic death of cancer cells and the Rb inhibitor increases the apoptosis inducing activity of mycolactome even in Rb positive cancer cells. The agent is specific to cancers in which Rb proteins are optionally expressed and mycolactome shows very strong anticancer effect in vitro as well as in vivo.
3364 CTATTGCAATCTGATATACTGTGTTGTTTTATAAAATTTTGCTTTTAATLAAALAAA 3423
                                                                                                                                                          3484 CAGAAIGIAAAAGAACIIACIGAITIIIIIIIIIAICAACITAAAIGAAAA +543
                                                                                                                                                                              3478 CAGAATGTAAAAGAACTTACTGATTATTTTCTTCATCCAACTTATGTTTTAAATGAGGA 4537
                                     3358 CIAITGGAATCIGATAIACIGIGIGIIIIIAIAAAAIITIGCIITTAATTAAATAAA 3417
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Human, retinoblastoma protein, Rb, syteolatis, sunst; apoptoois:
myrelacione; antisense; breast samser, bladder sunst; skin sameer;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 The invention relates to an anticancer agent comprising mycolactons
                                                                              3424 AGCIGGAAGGAAAGIAIAACOAIAIGAIACIACIACIAGIAGAAACAGAIIICAIAGGI
                                                                                                The present sequence is the human cDNA for retinoblastoma protein.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           stomach cancer, liver cancer, colon cancer, oral capity cancer;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Antimannon agent sects! for treatment of cancer e.g. of skin.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Sequence 4740 BP; 1508 A; 887 C; 862 G; 1483 1; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Human retinoblastoma protein cDNA sequence.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Example 4; Page 38-42; 44pp; English.
                                                                                                                                                                                                                                                                                                                                                                       ABK86079 standard; cDMA; 4740 BP.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        23-NOV-2000; 20000KR-0070089.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                     (first cntry)
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                                                                                                                                                                                                                                      3544 TTALTGATAGT 3554
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1501 ACCAGAAGTACATCACAAATCTTGALTCTGGAACAGATLIGTCTTTAACAATGTTIG 1560 2041 ATCATCTGGACCCTTTTCCAGCACACGCTGCAGAATGAGTATGAACTTCATGAGACAACT 2100 2161 CTTAAATTCAAATCATCTAACAGCATACAACGATCTCCTCATGCTGTLCAGGGAACAC 2220 2293 CTTAAATTCAAAATCATGTAACAGCATACAAGGATCTTCCTCATGCTGTTCAAGAGAC 2392 1201 ANICIGATITECTATITIAACAACIGCACAGIGAATCCAAAAGAAAGIATACIGAAAAGA 1260 1393 GTGAAGGATATAGGATACATCTTTAAAGAGAAATTTGCTAAAAGCTGTGGGACAGGTTGT 1452 1381 TCCATGCTTAAATCAGAAGAAGGATTATCCATTCAAAATTTTAGCAAATTTCTGAAT 1440 1441 GACAACATTTTCATATGTCIIIATTGGCGTGCGTCTTTGAGGTIGTAATGGCCACATAT 1500 1573 GACAACATTTTCATATCTCTTTATTGGCGTGCGCTCTTGAGGTTGTAATGGCCACATAT 1642 1561 ANTGECTIAATTIAAAAGCCTTEGATTITIACAAAGTGATCGAAAGTTTTATCAAAGCA 1620 1681 GAATCCCTTGCATGGCTCTCAGATTCACCTTTATTGATCTTATTAAACAALCAAANAAC 1740 1872 1860 1921 CAGAAGCCATTGAAATCTACCTCTTTCACTGTTTTATAAAAAA.GGTATGGTAGG 1980 2173 ATCATCTGGACCCTTTTCCAGCACACCTGCAGAATGAGTATGAATTGATGAGAGAGG 2232 1141 ATGAACATATCCAACAATTAATGATGATTTAAALTGAGAAGATGATGAAGTTTGAGAA 1200 1741 CGAGAAGGACCAACTGATCACCTTGAATCTGGTCTTGTCTTTAATCTTCCTCTCCAGAAT 1981 TATCTCCGCCTAAATACACTTIGTGAACGCCTTCTGICTGAGAPPPAGAATTAGAAPA 2233 CAPITTGGACCAAATTATGATGTGTFCCATGTALCCATALCCAAACTGAACAAAAA Š 3 5 5 цq Š **Q** ò 3 Š qq ολ q ζ ď οy q ò α Ω 9 ŝ qq ò . a ò 3 Š qq ò 9 à 3 ò a Ś ŝ

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3301 AAAATGGATATTATATTAGAAATTAGAAAATTACTAATTTTACACATAGATTTAA + 4460
                                       3433 AAAAAIGGATATTATTAGAAAITAGAAAAAAAITACTAATTTIACACATTAGAITTTATT 4492
                                                                                                                                                                           3553 AAAAGCTGGAAGCAAATATAACCATATGATCATCATACTAGTAACGAAAATTTCATA 4612
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       The probe can be used to detect tumour with an Rb detect equosteosarcoma, fibrosarcoma, soft tissue satcoma, small cell sarcoma, csp. of the lung, melanoma and mammary tumours.
                                                                                                                                                        3421 AAAASCTGGAAGCAAAGIATAACCAIATGAIACIAICAIACTACTACTACAAACASATTTCAIA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Deferting pro-disposition to develop - using retinublastoma gene probes to detect defects in the retinoblastoma.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Sequence 4579 BP; 1477 A; 843 C; 808 G; 1451 I; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Fung YKT, T'Ang A, Murphree LA, Benedict WF;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            (CLAY-) CLAYTON FOUNDATION FOR RESEARCH.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Probe, retinoblastoma; tumour; ss
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Claim 14, Page 17, 32pp, English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                     AAN81261 standard; cDNA; 4579 BP.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Probe for retinoblastoma gene.
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72	981	PTT FAAAAA TAAAGA PTAGA GGAAGA TATTI TI GGATGA TGATAAAAC FCTTGAGAG 	040
5 3	1041	DIATECTAFAGACIANTETTGAAACACAGAGAACACCAGAAAAAGTAACETTGATGAAGA 	1100
67 12b	10.00	OSTGAATGTAATTOTTOTACAOTOTAGTAAGTOTTATGAAAATTT 1 	160
五 皇	1161	AALGATTETAAATTEAAGAAGTGATEAAGGTEGAGAAATCEGATTECTATTETA T FILLETTETTETTETTETTETTETTETTTAA AA EGATGATTETAAATEGAGAGGATGAGAGAAAATCEGATTEGGATTETAA T	220 199
\$ <u>4</u>	1221	CAACTOCACAGAATCCAAAAGAAAGTATACTGAAAAGAGTGAAGGATAGATA	.280 259

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q ₀	1260	CTTTAAAGAAATTTGCTAAAGCTGT-GGACAGGTTGTGTCGAAATTGGATCACAGG-1418
ć	1341	ATACAAACTTGGAGTTCGCTTGTATTACCGAGTAATGGAAATCCATGTTAAAT7AGAAGA 1400
qo	1319	ATACAAACTTGGAGTTGGCTTGTTTTTTTTTTTTTTTTT
ć	1401	AGAAGGATTATCCATCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTCATATGTC 1460
qa	1379	AGAAGGATTATCCATTCAAAATTTTAGCAAACTTCTGAATGACAACATTTTTCATATGTC 1438
Oy	1461	TITATEGRANGERATORISADARI GIAATGACAAATALAGAGAAANAAA 1520
qq	1439	TTTATTGGCGTGCGCTCTTGAGGTTGTAATGGCCACATATAGCAGAAGTACATCTCAGAA 1498
o,	1521	TCTTGATTCTGGAACAGATTGTCTTCCCATGGATTCTGAAGGGCTTAATTTAAAAACC 1580
qa	1499	TCTTGATTCAGGAACAGATTGTCTTTCCCATGGATTCTGAATGTTAATTTAAAAGT 1558
ó	1581	CITTGATTITACAAAGIGATCGAAAGITTTATCAAAGGAGAAGGTGACAAGAGA 1640
da .	1559	CTITGATTITTACAAAGTGATCGAAAGTTITTATCAAAGGAAAGG
; 0y	1641	AATGATAAAACATTTAGAACGATGTGAACATGGATGGATG
q a :	1619	AATGATAAAACATTTAGAACGATGTGAACATCGAATCATGGAATCCTTTGCATGGCTCTC 1678
λo	1701	AGATTCACCITTATTTGAICITATTAACAATCAAAGGGGGGGAAGACCAACTGAICA 1760
qu	1679	AGATTCACCITTATTTGALCITATTAAACAATGAAAGGAPCGAGAAGGAPPAAATGATGATTA 1738
ć	1761	CCTTGAATCTGCTGTGAATCTCCTCTCAAAAAAACCTGCAGAAAAT 1820
qq	1739	CCTTGAATCTGCCTGTGCTCTTAATCTTGCTGTGCAGAATAATGAATG
Ċχ	1821	GLATICITICICCIGTAAGALGISCAAAGAAAAAGGIICAACTACGCIGTAAATICTAC 1880 HILLIITILIITIITIITIITIITIITIITIITIITIITII
qq	1799	GIATCITICICCIGIAAGATCICCAAAGAAAAAGGITCAACTACGCGIGAAATTCTAC 1858
ć	1881	TGCAAATGCAAAAACAAACTCAAGCCTCCAAAACAAAAGTTGAAATGTAC 1940
qc	1859	TGCAAATGCAGAGACACAAGCAACCTCAGCTTCCAGACCTAGAAGCCATTGAAATCTAC 1918
ć	1941	CICECTICACIGITITATAAAAAAGIGTATCABOTAACCIATCTCCABOTAAAAAATA 2000
qa	1919	CTCTCTTTCACTGTTTTATAAAAAGTGTATCGGCTAGCGTATCTCGGGCTAAATACAT 1978
ολ	2001	THEREFORE CHICKER AND A CONTROL OF THE STATE
qq	1979	TTGTGAACGCCTTCTGTCTGAGCACCCAGAATIAGAACAIAICAICIGGACCTITTCCA 2038
δλ	2061	GCACACOCDACAGAADGAGTATGAACTCATGAGAAAAAGCATTTGGAGCAATTATATAT 2120
qu	5034	GCAÇAPOTTOÇAĞARIĞAĞTATĞAAÇTÇATĞAĞAĞAĞĞÇATTIĞĞAPCAAALTATĞAT 2098
δ	2121	GEGITCCATCIATGCCAAAGCAAAGTGAAGAATATAGAGCTTAAAATFFAAAATFTTGT 2180
qu	2099	GTGTTCCATGTTTTTTTTTTTTTTTTTTTTTTTTTTTTT
ολ	2181	AAGAGGATATTTOTTGATGGTGTTGAGGAGATTGAAAGGGTGTTGAAAGAATTTGATGA
qq	2159	AACAGCATACAAGGATCITCCITCATGCIGITCAGGAGACAITCAAACAGGIIIIGAAAAA 2218
ςò	2241	AGANGAGGAGTATGTATTATAGTATTCTATAACTCGGTCTTCATGCAGGACTGA 2400
q 0	2219	AGAAGAGAGTALGATICIATIATAGIGTTOTATAACTOGTOTICATOTAGACACTGAA 2278
ς	2301	AACAAATATITGGAGTAGGTGCROCAGGCCCCTACCTGTCACATA 2.6.0
qq	2279	MATATITIGCAGIATGCTTCCAGCAGGCCCCTACCTTG CACCAATACTCACAT
ОУ	2361	5

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                                                                                                                                              2421 TATTTCACCCCCGAAGAGTCCATATAAAATTTCAGAAGGICTGCCAACAACAAAAAT 2480
                                                                                                                                                                                                                                              2398 TATLICAC/CCTGAGGTCCATATAAAATTTCAGAAGGTCTGCCAACACAAAAAT 2457
                                                                                                                                                                                                                                                                                                                                    Z481 DACTOCARDATICAAGAATOTTACTATTGATTGATTGATTGATTGAGTTGTGAGAGTTT
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     254] PSAGAAAATAAATCAGATGGTATGTAACAGGGACGGTGTGAAAAGAAGTGCTGAAAGG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Modified retinoblastoma tumoum suppressor, KTSP protein; cancer therapy;
3418 AACCHCATATGATACTACTGAAACAGAHTTCAFACCTCACAATGTAAAAGAAGT 4477
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    228 ITGGTTAACTTGGGAAAAGTTTCATCTGGGATGGAGTATGGGGAGGTTATATTGAAA 287
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                                                         3501 TACTGATTATTTTCTTCATCCAACTIATGTTTTTAAATGAGGATTATTGATAGT 3554
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             2; Indels
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                  Modified retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Claim 22; Page 142 147; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            cellular proliferation inhibitor; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Zhou Y;
                                                                                                                                                                                                                                                               AAV58441 standard; DNA; 3455 BP
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1269 CCGAGTAATGGAAATCCATGCTTAAATCAGAAGAAGAACGATTATGCATTCAAAATTTTAG 1428
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protein (RTSP) of the invention. The proteins can be used for inhibiting celliar proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
                                                                                                                                                       Modified retireblastoma tumpur suppressor. BISP protein, cancer therapy:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               ACTITITACTGACCTACAGAAAACATAGAAATCAGTGTCCATAAATTCTTTAATTLATA 411
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          292 AAGGAACTGTGGGAATCTGTATCTTTATTGCAGGTGGACCTAGGTGATATGTGGTTC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Match 95.1%; Score 3379.8; DB 19; Length 3392; Conel Similarity 99 9%; Pred, No. 0;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   inhibiting cellular preliferation, particularly cancer
                                                                                                                      Moditied relinoblastoma tumour suppressor gene.
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5 5	47z GALGLALIGHTEGATETHEAGAAALIGGA LELLHILLHILLHILLHILLHILLHILLH 410 GALGLATTGTTGGATTGGA	ACCACA LCLOAACT LALATATT CACA 	531 369
2 3	5.2. CAAPCAQPAGTEGATATETATETAAATAAA TTTTTTTTTTTTTTTTT		591 429
65 GE	592 ALCACATITIATIAGCIAAAGGGGAAGTAII. 	CAAATGGAAGATGATCTGGTGATTTCA 	651 489
5 g	652 TITCAGITAALGCIATGIGCTIGACIATII 1111111111111111111111111111111111	ALLAAACICICAOOTOCALGITIGUC 	711
5 £	712 AANGANCCATATAAANGAGGGGTTATACGGAT TITTITITITI 550 AAAGAAYGATATAAAACAGGGTTATAGGGAT	AALGGTLGACGTGGAACACCCAGGCGA 	771
5 E	772 BGTCRGANTABGAGTGCACBGATABCAAAACA HTTFTFTFTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	CTAGAAATGATACAAGAATTATTGAA H HIHHHHHHHHHHHHHHHH CTAGAAAATGAFACAAGAATFATTGAA H	831 669
5 3	B (2. OLICTCTGTAABAATA (GAALGTAATATAGA 	GAGGIGAAAAA EGTITATTIGAAAAAT HILLIHIHIHIHIHIHIHI GAGGIGAAAAATGTTATTIGAAAAAT	891 729
40 GF	892 THAIAPCHTHAIGAAHCHCHGGAGHGE HHITHHHHHHHHHH 7 WETHAACCHHAGAAHCHGAGCHGA	ACATCTAATGGACTTCCAGAGGTTGAA	951 789
5 g	952 AATCTTTCTAAACGATACGAAGAAATITAICT 	AAAAATAAAGATCTAGALGCAAGATTA 	1011 849
52 135	1012 HEFFEGATGATGAAAAGICTICAGAGIGA HEFFEFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	TCTATAGAGAGTTTTGAAACACAGAGA HILLIHIHHHHHHHHH TCTATAGAGATTHGAAACACAGAGA	1071. 909
5 £	1072 ACACAAAAADTAACTIDATGAAGAGDI TITTITITITITITITITITITITITITITITI SID ACACAAAAAGTAACCTIGATGAAGAGAGT	AALGTAATTGGLOOGAGAGTGGAGTT 	1131 969
5 £	11.12 AGGACTGTTATGAACACTATCCAACAATTAAT: 	ATGATTTTAAATTCAGCAAGTGATCAA 	1191 1029
5 3	1192 COLICAGAAADOLGALIICOTATIITAACAA 1111 HILLIIHIIHIHIHIHIHIHIHIHIHI 10-0) COTICAGAAAATGIGATIICOTATITAACAA	TOCACAGTGAATPCAAAAGAAAGTATA TTTTTTTTTTTTTTTTTTTTTTTTT	1251 1089
等 畫	1252 CTGAAAAGAGGAAGGATATAGGATACATCTT TTTTTTTTTT	AAAGAGAATTTGCTAAAGCTGTGGGA HTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	1311
85	1312 CARBETTGTGFGGAAATTGGAFCACAGAAATTGAAACHGGGATTGGGTTGTATTACGGA 13 FFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF	AAACITGGAGITGGCTIGIAFTACCGA HILLILILILILILILILILILILILI AAACITGGAGFTCGCTGTATTACCGA	1371 1209
\$ \frac{2}{5}	13/2 GLAADGAACCADCHAALCAGAGA - - - - - - - - - - - -	CGATTALCCATTCAAAALITTAGCAAA FELLITTITTETTTTTTTAGCAAA	1431 1269
5 3	1432 CHEGGARGACACHTHEALAIGEITH THEFFILETHEFILETHEETH	LTGGGGTGGGGTGTTGAGGTTGTAATG	1491 1329
5 3	1492 GPCMPATATAGRAGAAGTACATCTCAGAATCT 	GATTCTGGAACAGATTTGTCTTTCCCA 	1551 1389

οy	1552	TGGATTCTGAATGTGCTTAATTTAAAAGCCTTTGATTTTHACAAAGTGATGAAAAGTTTTT 1611	
qq	1390	IGGATICTGAAFGEGTIAAATTTAAAAGCCTTTGATTTTTACAAAGFGAFCGAAAGFTTT 1449	
9. 0. 0. 0.	1612	ATCAAAGCAGAAGGCAACTTGACAAGAAATGATAAAAATTTAGAACGATGTGAACAT 1671 	
o du	1672	CGAATCATGGAATCCCTTGCATGCTCTCAGATTCACCTTTATTGATCTTATTAACAA 1731 	
Oy Op	1732	TCAAAGGACCGAGAAGGACCAACTGATGAATCTGCTTGFCCTCTTAATCTTCTT 1791 HTTHEFTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	
م م م	1792	792 CTCCAGAATAATCACACTGCAGATATGTATCTTCTCCTGTAAAATCTCCAAAAAA 1851 HILIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	
yo Db	1852 1690	AAAGGTTCAACTACGGGTGTAAATTCTACTGCAAATGCAGACACACAAAAAAATTGTAAATTCTACTAAATGCAAAATGCAAAAAAAA	
Oy Db	1912 1750	TTCCAGACCCAGAAGCCALTGAAATCTACCTCTCTTCACCTTTTTALAAAAAGLGTAT 1971 	
dy D	1972	CGGCTAGCCTATCTCCGGCTAAATACACTTTGTGAACGCCTTCTGTCTG	
Oy Db	2032	TTAGAACATATCATCTGGACCCTTTTCCASCA'ACCTG'AGAATGAGTGAGTATGAACTCATG 2091	
Oy Db	2092		
ر ا ا		AATATAGACCTTAAAATCCAAAATCATTGTAACAGCATACAAGGATCTTCCTCATGCTGTT 2211 	
O, Dp	2212 2050		
Oy Db	2272	TATAACTCGGTCTTFCATGCAGAGGGCTGAAAACAAATATTTFGGAGTATGCTTCTACAGG 2331 	
م م م	2332	COCCCTACCTGCACCACAATACCTCACATTCCTCGAAGCCCTTACAGTTTCCTAGTTCA 2491	
à ć	2392	CCCTTACGGATTCCTGGAGGAACATCTATTTCACCCTGAAGATCATATAAAATT 2451	
Oy Db	2452	TCAGAAGGTCTGCCAACAACAAAATGACTCCAAGATGAAGAATGTTAGTATAAATT 2511 	
λο da	2512	GGTGAATCATTCGGGACTTCTGAGAAGTTCCAGAAAATAAAT	
à î	2572	GACCSTGTCAAAAAAAAGAGTGAAGGAAGCAAACCTCCTAAACCACTCAAAAAAAA	
g ç	2410	GACCGTGTGTGCTCAAAAGAAGTGCTGAAGGAAGCAACCCTCCTAAACCTTGAAAAAAATTA 2469	

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24.7.3 (GGTITHATATTGAAGATTPAATGAAGTAAGAAGTAAAGTAAAATLYBYYYAGAAGAAYPYY 2529
                                                                                                                                                                                                   24.92 AAATTTGAGGAGAAAGTGGGGAGAAATGACTTGTACTTGGAAGAGGGAATGGAAAAGCAGAAA 2751
                                                                                                                                                                                                                                                                                                                                                                                                      2530 AAATITCAGGAGAAACIGGCAGAAATGACIICIACIGGAAGAGGAATGGAAAAAGGGAAA 2589
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     2190 AFGAAFGATAGCATGGATACCTPAAACAAGGAAGAGAATGAGGATCTCAGGACCTTGGT 2649
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            2812 GGACACTGTGTACACCTCTGGATTCATTGTCTCTCACAGATGTGACTGTACTTTGGC 2871
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         2872 AGGITCTGTLFATGGCCACAPFLAATATCTTGAGCTCTTTTGTGGATATAAAAFGTGCA 2931
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This sequence encodes a modified relinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RISPs have a broader spectrum of
                                        suppressor, RTSP protein, caner therapy;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              268 GAGCTACAGAAAACATAGAATCAGTGTCCATAAATTCTTTAACTTACTAAAAGAAATT 327
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                61 GAACCCCGGGCACGGCGGCGGCGCCCTCATGAGAACCCAGAGGACCAGAGAAGAAGAAGAAGAACAGAGCT20
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      121 COGGAGACOTGOOTOTOTOTOAGOTTGAGT11GAAGAAAAAAAAAAACGGAAGTTTTACT 180
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     94.3%; Score 3351.6; DB 19; Length 3461;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Retinoblastoma suppressor protein with N-terminal modification
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  inhibiting cellular proliferation, particularly cancer
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Claim 22; Page 188-192; 249pp; English.
                             Modified retinoblactoma tumour suppre-
cellular proliferation inhibitor; ss.
                                                                                                                                                                                                                    Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Ha S, Xa H, Rhou Y;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             (BAYU ) BAYLOR COLLEGE MEDICINE
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      97US-0038118.
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                                                                                                                                                 Homo sapiens.
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	TAAACHCICACCICCATCHGCICAAAGAACA 720 TAAACHCICACCICCATGHGLILLILLILLI TAAACHCTCACCTCGATGTTGCTCAAACAACA 627 TGGTTCACCTCGAACACTGTCGCGAGGTCAGAAC 780 HILLIHIHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH	96 92 92 10 10 11 12 12	126 128 132 133 134 136 136 136
	66] ALGUTALGEGEGEGATALLITATES SEM ATGETATGEGEGEGTEGACTALLITATAL SEM ATGETATGEGEGTEGACTALLITATAL SEM ATGETATACCATTAA SEM INTERPRETAGAAAATAA ATGETATAGAAAATAGAAATAGAAAATAGAAAATAGAAAATAGAAAATAGAAAATAGAAAATAGAAATAGAAATAGAAATAGAAATAGAAATAGAATAGAATAGAATAGAATAGAAATAGAA	808 961 1021 928 1081 988 1141	1201 1108 1261 1168 1128 1288 1441 1348
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q	1408	AGCAGAAGTACATCAGAATCTTGATTCTGGAAGAGATTGGTTTTCCCATGGATTCTG	146.7
ς	1561	AAFGEGTTAATTTAAAAGGCTTTGATTTTAAAAGTGAAAGTTTTTAAAAGA	16.20
qq	1468	APPORTED FARTER AND CONTROLLED FOR AND CONTROLLED F	1527
λō	1621	621 GAAGGCAACTTGACCAAGAGAAATGATAAAAACATTTAGAACGATGTGAACATGGAGGTTG 168	1680
qu	1528	GAAGGCAACTTGACAAGAAAAAATGATAAAACATTTAGAACATGTGAACATGTGAATGTTG	1587
ΟŸ	1681	GAALGCCTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAAACAALCAAGC	1740
qu	1588	GAATCCCTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAAACAATCAAAGGA	1647
ΟŸ	1741	CGAGAAGGACCAACTGATGACGTTGAATGTTGCTTGTTTAATGTTGTGTGTAGAT	1800
qq	1648	CGACAAGGACCAACTGATGATGAAAGTGAAAGTGAAAAAAAA	1707
ò	1801	AATCACACTGCAGGAGATATGTATCTTTCTCTGTAAGATCTCCAAAGAAAAAAGGTTCA	1860
qq	1708	AATCACACTGCAGCAGATALGTATCTTTCTTCTGTAACATCTCCAAAGAAAAGGTTCA	1767
Óγ	1861	ACTRICCO GERAALTICERCEGGAAA EGGACACACAACAACCECAGCTECAGACC	1920
q Q	1768	ACTACGGGGGTAAATTCTACTGCAAATGCAGAGAACAAGCAAACTCAGCGTTCCAGGC	1827
ογ	1421	CAGAAGCATTGAAATCTACCTCTCTTTCACTTTTATAAAAAADDTATACTCTTTTCT	0851
a	1828	CAGAAGCATTGAAATCTACCTCTCTTTCACTGTTTTATAAAAAAGTGTATGTTTTTTTT	1887
Óγ	1981	TATCTCCGGCTAAATACACITTGTGAACGCCTTCTGTGTGTGTCTGAAAAAAA	2040
q	1888	FATCTCCGCCTAAATACACTTTGTGAACGCTTTTTTTTTT	1947
ογ	2041	ATCATCTCGGACCCTTTT CCAGCACACACTGCAGAATGAGTATGAACTAA DAGAGAAAG	2100
QQ	1948	ATCATCT GGACCT LICCAGCACACACGCAGAALGAGIAGAGAAGAAGAGAGAGAGAGAGAGAGAGAGA	2007
ΟŸ	2101	CATITIOGACCAANTATGATGITOTTCATCLATGGGATATGCAAAGTGAAGAATATAGAC	2169
q(1	2008	CATTTGGACCAAATTATGATGTGTTGCATGTATGGCATATGGAAAGTGAAGAATTAGGA	2067
λō	2161	CTTANATICANATGATEGIAACAGCATACAAGGATCTTCCTCATGCTGTTCAGGAGACA	2750
qo	2068	CTTAAATTCAAAATCATTGTAACACATACAACATCTTCTTCTTTTTTTT	2127
, o	2221	TTCAAACCIGTTTTGATCAAAGAAGAGGGTATGATTCTATTATAGTATTGATAAATTGG	7,780
qq .	2128	TTCAAACGTGTTTTGATCAAAGAAGGAGTTTTTTTTTTT	2187
φĄ	2281	CTCTTCATCAGAGACTGAAAAAATATTTTGAGTATGATTCACAGAGGCCCCTACC	2440
QC	2188	GICTTCATICCAGGGGCTGAAAGAATATTI TGCAGTATGCTTCTTTTTTTTTTTTTTTTTTTTTTTTTT	2247
ολ	2341	TTGTCACCAATACCTCACATTCCTCGAAGCCCTTACAAGTTCCCTAGTTCACCTTACAG	2400
q	2248	TTG!!CACCAATACC!!CACAT!!CC!CGAAGC?!!TAGAAGT!!IQ?!AGT!!TAGG	2 507
οy	2401	ATTCCTGGAGGAACALCTATATTTCACCCTGAAGACCTATATATAAAATTCAGAAGT	2460
qu	2308	ATTOCIGGGGGGGGGGTTTTTTTTTTTTTTTTTTTTTTTTT	2367
Οy	2461	CTGCCAACACAACAAAAATGACTCCAAGATCAAGAATCTTAGTATCAATTGAATCA	25.20
100	2368	CTGCCAACACAACAAAAATGACTGCAAGATCAAGAATGTTAGTATTTTTTTT	2427
ς	লে জুলি	TEGGGAACTICIGAAAATICTAAAAAAAAAAAAAAGAAGAAGAAAAAAAAAA	2580
00	2428	TTCGGGACTTCTGAGAAGTTCCAGAAATAAATCAGATGGTATGTAACAAGAGGTGTGT	2487
ολ	2581	CTCAAAAGAAGTGCTGAAGGAAGCAACCTOOLAAAOCAOTGAAAAAAATAOTTTGAT	2640
qq	2488	CTCAAAAGAAGTGCTGAAGGAAGCAACCCTCCTAAACCACTGAAAAAACTACCTTTGAT	2547

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2201 OAGAAA/TGO/AGAAATGA/TTCTACTCGAACAGGAATGCAAAAGGAAAAAGAAAATGATGAT 2760
                                                                                                                   ZEOROSTAGARARITGGGGAGARATGACTICTACTICGAACACGAATGCAAAAGCAGAAAATGAATGAT 2667
                                                                                                                                                                                  Z 11 FORTALOGALAGE FCAAACAANGAANAAATBAAGATETAGAACAOFTFOGTIGGAOAGTGF 2820
                                                                                                                                                                                                                                                                                                                                                                       28%; ITALGGCCACATITAATATCTICAGCICITITITGIGGAIAIAAAATGTGCAGATGCAATT 2940
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   2966-AATTGCTGTGYTTTATGGATAGTAAGAATGGGYYTTAGAGGFGGGAGTGYTGATAAYAAGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               312. COLGICLIGACIACITH GCCONCOLONG NACATATAGGTGANGTOTGCTCONGTONATAL 3180
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        *IH! TAATTTATATGTATATTTTTTTAATTTAACAGAAAAGOGGIAGAAAATGTGTGTATGT 3240
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  241 ATCITCCAAATGCAATTGAATGACGGCCAITCACCAAAATTATCCTGTCTGTGT 3300
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              $148 AUCTICOAAAIGCAAIIIGATIGACTGCCCAIIICAACAAAIIAICCIGAACTCIICEGC $207
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     34.1 TTACTATIGGAAICIGATATACIGIGGTIGTTTTATAAAATTTTGCTTTTAATTAAAT 3420
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  9421 AAAAGCTGGAAGGAAGTATAAACCATATGATAGTAATAATAAGAAGTGAAAAGAGAITICATA 3480
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          432* AAAAGCIGGAAGCAAAGTAIAACCAIAIGHHHHHHHHHHHHHHHHHHHHHHHH
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                                                                                                                                                                                                                                                                                                                                                                                                                   2788 IIAIGGGGAGAIITAATAIGIIGGGCIGTITTIGGGAIAIAAAAIGIGGAGAIGGAAII 2847
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                                                                                                                                                                                                                                                                               28.21 GTACACHTCTGGATTGATTGTCTCTCACAGATGTGACTGTATAACTTTCCCAGGTTCTGT
                                                                                                                                                                                                        AAV58443 Standard, DNA, 3323 BP.
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This sequence encodes a modified retinoblastoma tumour suppressor protein (RTSP) of the invention. The proteins can be used for inhibiting calbular proliferation, when coadministered with a p53 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The PTSPs have a broader spectrum of activity than wild type RTSPs.
                                                     Modified retinoblastoma tumour suppressor; RTSP protein; cancer therapy;
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Local Similarity 99.9%; Pred. No. 0;
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               Modified retinoblastoma tomour suppressor gene.
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                                                                        proliferation inhibitor; ss.
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οy	2700 GC	AGAAACTGGCAGAAATGACTCTACTCGAACAGCAAAAGCAGAAAATGAATG
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AAV58441 standard; DNA; 3455 BP AAV58441; RESULT 1 AAV58441

ALLEINMENTS

Modified retinoblastoma tumour suppressor gene.

02 DEC-1998 (first cutry)

Modified retinobiasiona implicasor: Kish profess; rancer therapy; cellular proliferation inhibitor; ss.

Homo sapiens.

Location/Qualitiers 7..2644 56.94 /*tag-

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This sequence encodes a modified retinoblastoma tumour suppressor protein (RTSP) of the invention. The protein can be used for inhibiting cellular proliteration condministered with a pr3 protein. The preparation he used for treating diseases characterised by abnormal cellular.
                                                                                                                                                                                                                                                                                                                                                                                                                                                            proliferation, particularly cancers. The RTSPs have a broader spectrum of activity than wild type RTSPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      67 GAACCIGATTTTACTGCATTATGTCAGAAATTAAAGAIAGCAGATGATGTCAGAGAGA 126
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  SerPhethaPhethrGluLeuGluLysAsnatleGluTleSerValHisLysPhePheAsn 100
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    247 TOUTICACITITACTGAGCTACAGAAAAAGATAGAAAATGAGTGGGAYAAATTGTTAAC 306
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       121 LeuleulysGlulleAspThrSerThrLysValAspAsnAlaMetSerArgLeuleulys 120
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       41 AlaTrpLeuThrTrpGluLysValSerSerValAspGlyValLeuGlyGlyTyrIleGln 60
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                1 MetGlnAspSerGlyProGluAspLeuProLeuValArgLeuGluPheGluGluThrGlu 20
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Retinoblastoma suppressor protein with N-terminal modification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Sequence 3455 BP; 1153 A; 631 C; 627 G; 1044 T; 0 other;
                                                                                                                                                                                                                                                                                                                 inhibiting cellular proliferation, particularly cancer
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                                                                                                                                                                                                              Hu S, Xu H, Zhou Y;
                                                                                                                                                         (BAYU ) BAYLOR COLLEGE MEDICINE
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                       547 ATTICALITICAGITAATGCTATGTGTCCTTGACTATITTATAAACTCTCACCTCCCATG 504
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                                                                                                                                                                                                                                                                            667 AGGGGGGTTAGAATAGGAGTGCAGGATAGCAAAACAACTAGAAATGATACAAGAATT 726
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161 SerTrpIleThrPheLeuLeuAlaLysGlyGluValLeuGlnMetGluAspAspLeuVal
                                                                             181 HeSerPheCInLeuMetLeuCysValLeuAspTyrFheHeLysLeuSerProProMet
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                                                                                                                                                                                                                                        221 ArgArg61y61nAsnArgSerAlaArgIleAlaLys61nLeuGluAshAspThrArgIle
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42 TrpLeuffirfrpGlufysValSerSerValAspGlyValLeuGlyGlytyrffedfulys 61
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Gene is taken from human chromosome 13q14 retinoblastoma (RB) cDNA. By installing a working CSG, safe and specific treatment and prophylaxis can be given to cancer patients.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Controlling cancer - by replacing ineffective cancer suppressing qene with cloned.
                                                                                                                                                                                                                                                                                             Cancer; cancer supressing gene; CSG; 14g14; retinoblastoma;
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139..2922
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                                                          AAQ04713 standard; cDNA; 2994 BP
                                                                                                                                                                                                                                   Cancer supressing gene (CSG)
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                                                                                                              AAQ04713;
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3 3	1.4.2	TyrAsoValLeuPheAlaLeuPheSerLysLeuGluArqThrCysGluLeuIleTyrLeu	141
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40 20	142	ThighnproSerSerSerTleSerThrGlulleAsnSerAlaLeuValleuLysValSer 	161 720
5 G	16.2	TEPTIET IN PRECENTANTAL ASCING LIVATE LENGT IN MATERIAS PASPIEUVATITE GOALCH AND TANDARD T	181
ŝ:	182	SerPhedluLeuMetLeuCysV31LeuAspTyrPheTlefysLeuserPrePreMetLeu	201
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5 3 5 3	242 961	GLUVATLENGYSELYSGEUSELSGESABNITTARASPGEUVALEFGASNAVALTYFFREELYS 	261 1020
45 65	262	AshPhelleProPheMetAshSerLeadlyLeuValThrSerAshGlyLeuProGluval 	
5 4	242	Cluashicuseriysarqiyrcluclulletyricusysashiysasplenaspalaarg 	301
5 =	362	LeurhetenAspiliaAsptysThrLeudlnThrAspSerIleAspSerPhedluThrGll	
5 G	1221	ArgibirProArgiysSerAsnicuAspGluGluValAsnVallleProProHisThrPro	341 1260
5 8	342	Valargihrvalmetasufbrilegindinkeumetilekeuasnseralaserasp 	361 1320
2 €	362	GIDPTOSerGludsnLevIlleSerTyrPheAsnAsnCysThrValAsnProLysGluSer 	381 1380
ži di	382		401 1440
5 3	462	GLyGLBGLyCysValGlbLIGCLySerGInArgTyrLysLcuClyValArgLcuTyrTyr 	421 1500
3 <u>을</u>	1501	AraValMetGluserMetLeuLysserGluGluGluArgLeuserlleGlnAsnPheser FILLELLELLELLELLELLELLELLELLELLELLELLELLE	

1981 AAAAAAAGITTCAACITATGGGTGTAATTTGTAGTGCAAATGCAGAAGAAAGGTGA 2040 2581 ATTTCAGAAGGTCTGCCAACCACAAAAATGACTCCAAGATCAAGAATCTTAGTATCA 1561 AAACIICIGAAIGAAAAAIIIIIGAIAIGICIIIAIIGGGGIGGGGICIIGAGGIIGIA 1620 2281 AAGAATATAGACCTTAAATTCAAAATCAITGTAACAGGATACAAGGATCTTCCTCATGCT 2340 _ 2∝ 2 782 IleserGluGlyLeuProThrEysMetThrProArqSerArqIleLeuValser 801 502 PhotletysAlaCluGlyAsnLeaThrArgCluMct.1.clysHisLeuCluArgCysGlu 521 582 LysLysGlySerThrThrArqValAsnSerThrAlaAsnAlaGluThrGlnAlaThrSer 601 602 AlaPheqluThrdlutyaProLeuLysSerThrSerLeuSerLeuFheTyrLysVal 621 642 GluLeuGluHisIleIleTrpThrLeuPheGlnHisThrLeuGlnAsnGluTyrGluLeu 641 KK2 MetAngAspAngHisLouAspGinIleMetMetSysScrMctIyrGiy1leGyStysVal 681 682 lysAsmileAspleutysPhelysIlelleValThrAlaTyriysAspleufroHisAla 701 762 SerProLeuArgIleProGlyGlyAsmIleTyrIleSerProLeuLysSerProTyrLys 781 442 lysteuteuAsnAspAsnIlePheHisMetSericuteuAlaCysAlaixuGluValVal 451 802 HoffyGluserPheGlyThrSerGluTysPheGlnTysHeAsaGlaMetVal77sAsu 821 542 GinSertysAspArgGluGlyPrcThrAspHisLeuGluSerAlaCysProLeuAsnLeu 722 PheTyrAssSerValPheMetGlnArqLeuLysThrAsnIlcLeuGlnTyrAlaSerThr 562 ProLeuGinAsnAsnHisThrAlaAlaAspMetTyrLeuSerProValArqSerProLys 482 ProTrplleLeuAsnValLeuAssLeuLysAlaFheAspFheTyrLysVallleGluser qc á QQ qq 임 qq qq qq ηď ó qu ά òγ δò ά Ö.; ò 6 ò. δλ 3 οy á ŝ ō, ζ ò

Sequence 2994 BP; 974 A; 618 C; 594 G; 808 L; u other;

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It is also compatible with other methods and devices tor requiating ectain physiological processes of the body, such as blood cell produ, and sameter produ. Fragments of the protein are soluble in low concus, of alyerol thus enhancing their value in
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protein RB (see AAM62465). A new claimed polypeptide is a fusion of:
(i) a transcription factor (PP) comprissing a DNA binding domain,
and (ii) a retinoblastema (Rb) polypeptide that includes a growth
suppression domain. Also new are: (I) a nucleic acid encoding the
fusion protein, and (2) expression vectors containing such DNA.
The tusion protein, particularly expressed from quer therapy
rectors (especially adenovirus vectors), is used to treat
hyperprofiterative conditions, specifically career (particularly of
the bladder) or restrems; datter anapoplasty), but also diabetic
telinopality, thyroid hyperficials, Grave's disease, proclasts,
benium prostatic hypertrophy, Li Fraumeni syndrome and peripheral
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     vascular disease. Tissue specific expression of FP-RF lasions is provided. The Dusion proteins are more effective in repressing transcription of the EZF promoter than Rb alone and cause cell-cycle arrest in a Mailety of cells.
                                                                                                                                                                                                                                                                                                                                                                       This nucleotide sequence includes a coding region for retinoblastoma
                                                                                                                                                                                                                                                        used to
                                                                                                                                                                                                                                                    New Insion polypeptide of, e.g. transcription factor—use
treat, e.g. hyper proliferative disease such as cancer and
restenosis
                                                                                                                                                         Antelman L. Gregory RJ, Wills KN;
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                  97WO US21821.
                                                       970S 0801092.
960S 0751517.
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                                                                                                                 (CANAL ) CANALL INC.
                                                                                                                                                                                                              P PSDB: AAW62465.
                13 NOV 1997;
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Sequence 2994 BP; 974 A; 618 C; 593 G; 809 T; 0 other;

Alliquinent Scores:

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This sequence represents the wiid type human retinoblastoms gene. The invention relates to a method of detecting a mutated retinoblastoma (PBB) nucleic acid in mammals comprished hybridizing an isolated full-length, whid-type RB (WERB) CDRA probe to a cell sample and detecting a mutated RB nucleic acid. The method is useful as a diamostic tool for diagnosting retinoblastoms. RB cink of genomic DNA are preferably used as probes to determine the discussion of the mRB gene through genomic DNA blotting analysis or using the method of restriction transment bright polymentalized to generate specific anity RB prosecus and letter consists which are useful of innonvaccucing of tissue biopsy. The diagnostic method is particularly intended for use in screening
                                                                                                                                                                                                                                                                                                                                                     RB gene; human; retinoblastoma gene; mutation detection; immunoscreening;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 cancer, such as, osteosarcoma, librosarcoma, glioblastoma, breast cancer whether or not connected with retinublastoma. The method is also used in the suppression of tumbourigenesis where the absent RB protein ppRBHIO will be provided through the mojecular induction and gene
retinoblastoma diagnosis, hereditary retinoblastoma, secondary cancer; osteosarcoma; fibrosarcoma; glioblastoma; breast cancer; tumouriyenesis suppression; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          families with a history of hereditary retinoblastoms and for screening their children. It may also be used in prophylactic and postnatal screening and for the prediction of the development of secondary
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                transplanting of the RB cDNA to the individual in need of ppRB110.
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                                                                                                     2881 AAAATGAATGATAYATGATAGCTCAAACAAGGAAGAAAA 2922
                                                                               882 LysMetAsnAspSerMetAspThrSerAsnIysGluClys 895
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Detecting retinoblastoma gene cancer in mammals
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	22	ProAspPhrThralaLeuCysGlnLysLeuLysTleProAspHisValargGluArgAla 4 	41
	4.2	Trete ithetre-laugsvalserse-valaspolyvallenglyglytrileglaugs 	51 420
	6.2 4.2.1	LystyschulentroclyttesysttephertealaalavalaspeluaspelumetSer 	81 480
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	262 1021	AsibPreTieProPheMetAsinSerLeuGlyLeuValThrSerAsinGlyLeuFroGluVal :	281 1080
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2221 ATGAGAGAGAGATTTGGACGAATTATGATGTGTTYALGTATYNALATGAAATG 2280 2041 GCCTTCCAGACCCAGAAGCCATTGAAATCLACTCTTTTCACTGTTTTATAAAAAAGTG 2100 2101 TATCGGGTAGGGTATGTGGGGGTAAATACACTTIGTGAAGGGGGTTGTGTGTGTGAGTAGTGA 2150 1381 ATACTGAAAAGAGTGAAGGATAGGATACATGTT FAAAGAGAAATTTGCTAAAAGTGTG 1440 1681 CCATGGATTCTGAATGTGCTTAATTTAAAAGGCTTTGATTTTTAAAAGGGTT740 1741 TTTPATCAAAGCAAGGGAAGGTTGACAAGAGAAAIGAIAAAAGAITIAGAACAIGIGAA IBOO 1921 CCTCTCCAGAALAATCACACTGCAGCAGATATGTATGTTTCTCTCTGTAAGATCTCCAAAG 1980 58.I 422 ArgValMetGluSerMetLeuf.ysSerGluGluGluArgLeuSer11eGlnAsnFheSer 441 442 LysLeuLeuAsnAspAsnIlePheHisMetSerLeuLeuAlacysAlaLeuGluValVal 461 542 CluserLysAspArgCluClyProThrAspHisLauGluSerAlaCysProLeuAsnLeu 561 642 GlufeuGluHisilelleTrpThrLeuPheGlnHisThrLeuGlnAsnGlu1yreHulæn 661 382 IleLeuLysArqValLysAspileGlyTyrilePheLysCluLysFheAlaLysAlaVal 401 502 PhelleLysAlaGluGlyAsnLeuThrArqGluMetlleLysHisLeuGluArqCysGlu 521 582 Lyst.ysClySerThrThrArqValAsnSerThrAlaAsnAlaGluThrGluAlaThrSer 601 602 AlapheGlnThrGlnLySProteutySerThrSert.cuSert.cuPatyrtyStySVal 621 622 TyrArqLeuAlaTyrLeuArqLeuAsnThrLeu:/ysGluArqLeuLeuSerGluHisPro 641 522 HisArglleMetGluSerLeuAlaTrpLeuSerAspSerProLeuPheAspLeulleLys 362 GInProSerGluAsnLeufleSerTyrPheAsnAsnCysThrValAsnProLysGluSer 482 ProTrp11eLeuAsnValleuAsnLeuLysAlaPheAspPhe1ytLysVallHevHuSer 342 ValArgThrValMetAsuThrlleClnGlnLeuMetMetlleLeuAsnSerAlaSerAsp . o. qq <u>a</u> q q ò <u>q</u> g a ò q ô 00 ò a ογ g 5 $^{\circ}$ q ò ŝ <u>1</u> $\dot{\circ}$ g ò ô q ò ò ŝ 5 ŝ

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1.2 Valbach The PhelycansVallesTatelysGhGlustafyrAspRecileTieVal 721
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2441 GHCACCACACACACCTTYCAAAGAAGAGAGTATGATYCTATCTACTA 2400*
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adenovirus expression vector, where the vector has an insert of exogenous DNA comprising a gene encoding a foreign protein and adenovirus DNA is which all of the coding sequences of Pla, Flb, and protein IX, and part of E3 are deleted. The vectors are useful in gene therapy treatment of concer, especially for treating p53 delicient tumours. The vector enables safer and more efficient gene therapy of
                                                                                                                                                                                                                       The present invention describes a composition comprising a recombinant
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    721 TGGATGACATTTTATTAGCTAAAGGGGAAGTATTACAAATGGAAGATGATGTGGTGATT 780
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        182 SerPheGliLeuMetLeuCysValLeuAspTyrPhoIleLysLeuSerProFroMetLeu 201
                                                                                                                                                                                                                                                                                                                                         cancer. The present sequence encodes human pil0-RB retinoblastoma tumour suppressor which can be used as the foreign gene in the above
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   2 GlnAspSerGlyProGluAspLeuProLeuValArqLeuGluPheGluGluThrGluGlu 21
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Recombinant adenovital vectors useful for gene therupy of cuncer.
                                                                                                                                                                                                                                                                                                                                                                                                          Sequence 2995 BF, 975 A, 618 C, 593 G, 809 T; 0 other;
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Mismatches:
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                                                  Wills KN;
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              (CANJ-) CANJI INC
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:- <u>2</u>	242	GLUVATLOSUŽSKŲSGLUCISASALTICASPGLUVATLYSASDVATTYFPROLSS TELETHI FELLITITITITITITITITITITI GAAGITGLGGIAAAGAAGAAGGAAGGIAATATAGAGGGGAAAAAGGITATTCAAA	261 1020
ي ج	1021	Asorpho-Hepropho-Motasoser[JouglyLoughyLough]	281 1080
<u>ب</u> ج	282	GLUASBILGESCLIJSAFGLYFGLUSTGJTCHLYSASBILGESSPLCHASPALAAFG 	301 11 4 0
≽ .⊋	102	LouthedouasplisasplysthrieuGinthraspserfleaspserthedinthriti 	321 1200
is a	122	ArqThrProArqLysSvrAsuLeuAspGluGluValasuVall1PProProBisThrPro- 	341 1260
> - A	142	ValarqihrValMetashihrileGinGinLeuMetMetileLeuAshSeralaSeraspillililililililililililililililililili	361 1320
5 2	16.2	GIRPLOSCEGLUASDECULLESCETYFPHCASDASDCYSTHEVALASDPFOLYSGLUSCE HTH FELLER HTH HTH HTH HTH HTH HTH HTH CAACTTCAGAAAAAAAAAAAGTCCAAACTTCAGAAAAAAAA	381 1380
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× 4	402	GLPSTEGT POYSVALCTO TO SOFGINATELY TYSTSCOCTYVALAR GLCGT PTTYF OF THE FILE OF	421 1500`
μ	1501	ArqvalMetGluserMetLeviLysSerGluGludluArqrauserHeGluAsnPheSer 	441
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AAX00737 standard; cDNA; 2995 BP

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CONA encoding a retinoblastoma profein designated ppRR-110 or pll0-RR
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                                                                                                                                                  Retinoblastoma protein; RB protein; ppRB-110; p110-RB; inhibition;
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                                                                                                                                                                                proliforation; cancer; retinoblastoma, secondary osteosatcoma, broast cancer; small-cell lung cancer; fibrosarcoma; ss.
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Recombinant ademovirus expression vector comprising a partial or total deletion of a protein IX DNA and a gene encoding a foreign protein e.g. suicide protein, useful for inhibiting or reducing the proliferation of
                                         2401 YTCTAFAACTCGGTCTTCATGCAGAGACTGAAAACAAATATTTTGCAGTALGCTLCCAGC 2460
                                                                                                                                                         2581 ATTTCAGAAGGTCTGCCAACAACAAAAAAGACTCCAAGAATCAAAAATCLTAGTATCA 2640
                                                                                                                                                                                                                                                                                                                                       2821 ICCAAATITCAGCAGAAACTGGCAGAAATGACTTCTAGTCGAACGAATGCAAAAGCAG 2880
                                                                                                                                 842 LeuArqPheAspIleGluGlySerAspGluAlaAspGlySerLySHisLeuFiglyGly 861
                                                                                                                                                                                                                                                                                                                  862 SerlysPheGlnGlnLysLeuAlaGluMetThrSerThrArgThrArgMetGlnLysGln 881
722 PheTyrAsnserValPheMetGlnArqLeuLysThrAsnileLeuslalyrAlaSerThr 741
                                                                                                                                                                                                                          822 ScrAspArgVall.cul.ysArgScrAlaGlaGlgSerAsnProProLysProLoul.ysLys
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Retinoblastoma: tumour suppressor protein; Rb: p53; cancer; adenoviral vector; qene therapy; thymidine kinase; ds.
                                                                                                                                                                                                                                                                                                                                                             Retinoblastoma tumour suppressor gene.
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94US-0246006.
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19 MAY 1994,
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Loreign protein. This vector can be used in gene therapy, particularly to introduce tumour suppressor genes into cancerous cells Genes which may be used include p53, thymidine kinase and relinchiastoma tumour suppressor yene (Rb). The present sequence is the retinoblastoma tumour
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                                                                                          the present invention describes an adenoviral expression vector comprising a deletion in the protein IX gene and a gene encoding a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           2 GlnAspSerGlyProGluAspLeuProLeuValArgLeuGluPheGluGluThrGluGlu
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Best Local Similarity:
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282 GluAsmieuSeriysAraTyrdludludviythemiyoAsmiyoAsplemAspAlaAra
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Retinoblastoma; RB; tumour suppressor protein; pl10kB; p53; gene therapy; cytostatic, antithyroid; autipseriatic; adenovital protein IX; pseriasis; thyroid hyperplasia; draw's discess; heparocellular cercinoma, neoplasm; benium prostatic hypertrophy; Li-Fraumeni syndrome; sickle cell anapmia; Tay Sachs disease; leukaemia; lymphoma; adenovirus vector; cancer; ss.
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The present cDNA sequence encodes retinoblastoma (RB) tunnour suppressor. The invention relates to a recombinant adenovirus expression vector characterised by the partial or total deletion of the adenoviral profein IX DNA beginning at nucleotides 457 or 460 and ending at 4020-4050, and having a gene encoding a loreing profein such as tumour suppressor profein, such as tumour suppressor quies useful to the agent in useful for treating in gene therapy. The vector is particularly useful for treating or reducing hyperpoliterative relificationals such as thyroid hyperplasia, Grave's disease, psoriusis, benign prostatic platar catchona, prepiasms, leukarmias, lymphomas, etc. to
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         inhibit tumour proliferation or to ameliorate particular related pathology such as sickle cell anaemia and lay Sachs disease. The vector is also useful for the safe recombinant production of diadnostic and
                                                                                                                                                                                                                                                                                                                                                                                                   New recombinant adenovirus expression vector having a gene encoding for a foreign protein and a partial or total delection of the adenoviral protein ix DNA, useful in gene therapy for treating or reducing hyperproliferative cells.
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                                                                                           "Retinoblastoma tumour suppressor protein.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Sequence 2995 BP; 975 A; 618 C; 594 G; 809 T; 0 offier;
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                                             Location/Qualifiers
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Retinoblastoma; tument suppressor protein; pll0-RB; cell cycle; p53; Rb; mitosin; cell death; adenoviral protein LX; gene therapy; cytostatic; adenovirus expression vector; tument; non-small cell long cancer; small cell lung cancer; hepatocarchioma; hepatocallular carcinoma; melanema, retinoblastoma; coloreital carcinoma; astrocytoma; qlioblastoma; neuroblastoma; ovarian carcinoma;
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The present invention describes a recombinant adenovirus expression vector, which comprises a partial or total deletion of a protein IX DNA and a gene caroding a foreign protein. It is recombinant adenovirus vector teaching to a seed to determine a suppression vector is particularly useful for treating or suppression vector is particularly useful to treating or suppressing proliferation of a tunnour, e.g. non-small cell lung cancer, small cell lung cancer, melanoma, retinoblastoma, breast tunnour, colorectal carcinoma, melanoma, retinoblastoma, breast tunnour, colorectal carcinoma, sarcoma prostate tunnour, bladder tunnour, tunnour of the retinoblastochlastoma, described as transception and retail cancer observed as encodes the retinoblastoma tunnour suppressor protein plum RK, which is
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protein (RTSP) of the invention. The proteins can be used for inhibiting cellular profiteration, when coadministered with a p54 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular.
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                                                       Location/Qualitiers
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They can be used for the production of proteins such as tumour suppressor proteins which can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers.
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                                                                                                                                                                                                                                                                                                        Minimal promoter, tetracycline responsive expression vector, IREV: transcriptional transactivation domain, IID, tetracycline repressor protein, TRE, tetracycline operator; production, stable cell fine; protein production,
2689 TCCAAATTTCASCAGAAACTGGCAGAAATGACTTCTACTGGAACGGAATGCAAAAGCAG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           New Letracycline responsive expression vectors—used for the
Lightly controlled expression of genes, such as tumour suppressor
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                                                                                      882 LysMetAspAspRerMetAspThrSerAspLysGluGluLys 895
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tumour suppressor protein; treatment; cancer; ss.
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Mismatches:
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                                                                                                                                                                                                                                                                                                                                                                                                                                                    Location/Qualifiers
                                                                                                                                                                                                                                                                       DNA sequence of the specification,
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hESI2; telomerase; catalytic subunit; reverse transcriptase; life-span; reficeblastoma; p53; tumour suppressor; intibitor; arteriosclerosis; profiferation; immortal; tumour therapy; macular degeneration, activator,
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2.2 PhelyrAsuSerValDhoMottlnArgiouTysThrAsnilgiouGinfyrAlaSerThr 741
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in treating age related diseases

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Include cdk4 or cdk6 mutants. In particular, a cdk4 mutant is one which dillors from at one or more of residues R22, 824, 885 and/or 597.

Additional constructs include a papilloma virus E7 protein, or other viral oungeration which Pspasara F9 and/or F57. Antisense anathrated the Rb and pl61NK4a genes may also be used. The cclls are subsequently of proliferative capacity of cclls. The cclls are subsequently of use in pharmaceutical and cosmetic preparations used to read conditions related to (Fremative) against eq. marvular degeneration and arteriosclerosis. The cells can also be used to replace tumour cell lines in vitra and for studies or licherial and physiological agents.
                                                                                                                                                      The invention concerns methods and recepture for extending the life span, e.g., the number of mitolic divisions, of a cell. The method relies on activities of a telementary activity and inhibition of one or both of a rethoblastoma (Rb/NNK4 pathway or a p53 pathway. Phosphorylation of k by cyclic dependent kinases, cake and cake, releases the cells into the division cycle. Binding of INK4 pad add cake, releases the cells into the approximation p10 fNK4a, iditalies kinase detainty and resembly inactivate an arrest. Be inactivates an selectively and reversibly inactivate an Rb/INK4 pathway. Reposited a Rb/INK4 pathway. The oncoprotein MDM2 is a cellular inhibitor of Rb/E2P function and the p53 tumons superssorted can did can also be used in the methods. Other molecules which can be used.
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designated as Andregen receptor respectivator proteins from the present invention can be used in screening assays to identify candidate pharmaceutical molecules for the ability to promote or inhibit the interaction of androgen receptors ability to promote or inhibit the modulate andreamic activity. The identification and characterisation of androgen receptor such as those of the invention will
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/note- "androgen receptor coactivator"
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                                                                                                                     AAX88444 standard; cDNA; 4839 BP.
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                    242 CluValLouCystysCluHisGluCysAsnileAspCluValLysAsnVālTyrPluLys 261
                                                                                         20 AAAAAGGAAGTGTGGGGGAAATGTGTATGTGCAGTGAGTTGACCTAGATGAGATGTCCG 479
                                                                                                                                                                               102 LeuLysGlufleAspThrSerThrLysValAspAsnAlaMetSerArgLeuLeuLysLys 121
                                                                                                                                                                                                600 TATGATGTATTGTTTGGATTGTAGGAAATTGGAAAGGAAATGGTGAACTTATATATTTG 659
                                                                                                                                                                                                                                                                                                 142 ThtGLiiProSerSerSertleSerThrGlulleAsnSerAlaLeuValLeutysValSer 161
                                                                                                                                                                                                                                                                                                               182 SerPheClnLeuMetLeuCysValLeuAspTyrPhelleiysheuSeiFroProMetLeu 201
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42 TrpLeuThrTspGlotysValSerSerValActSLyValLeuSlyGlyTyrJleSLuLzo 61
                                                             62 lystysClutcuTrpClyffeCysflcFheffeAlaAlaValAspteuAspGluMetSer 81
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Human, cancer, colon, breast, ovary, oesophagus, kidney, thyroid,
stomach, lung, prostate, pancreas, carcinoma, antitumour, cancerous,
cytostatic, gene therapy, antineoplastic, Wilm's tumour, adenocarcinoma,
842 LeuArqPheAspileGluGlySerAspGluAlaAspGlySerLysHisLeuBroGlyGlu_B61
                                                                                                                                          802lle<br/>GlyGluSerPheGlyThrSerGluLysPheGluLysIleAsnGluMetVal<br/>CysAsn\#21
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20000S-235711P.
20000S 235720P.
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2000US - 245647P.
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2000US-235863P.
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(AVAL.) AVALON PHARM.

Audustus M., Carter FC, Ebner P., Endress G, Horrigan S; Weaver Z; Young PE, Soppet DR,

WPI: 2002-188264/24.

Screening for anti-neoplastic agent involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, and determining a change in expression of a gene of a signature gene set

.aim 1; SEc 1D 1210; 44pp; English.

The present invention describes a method (MI) for screening for an unit neoplastic agent. The method invelves exposing cell or a change in explastic activity, determining a change in expression of at least one dem (i) of a signalure gene activity where (i) comprises a sequence (S) selected from 8447 sequences (given in ABL61664 to ABL7010), or is at least 4% identical to (S) where a change in expression is indicative of actioned lastic activity. (I) has expositive expension is indicative and encoplastic activity. (I) has expositive activity and can be used to receive an anti-neoplastic agent, and can be used for screening an anti-neoplastic agent, and can be used for producing a product which is the data collected with respect to the anti-neoplastic agent as a first of M, and the data is sufficient to convey the chemical structure and a second as colon, breast, stomach, lung, thyroid, oesophaueal ovarian. Ridney, prostate or paecreatic cunner adenocarcinoma, carcinoma, clear cell cancer, infiltrating ductal cancer, infiltrating lobular cancer, squamous egil carcinoma, neutomodocrino vareinoma, papillary carcinoma and Wilm's tumour.

Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other;

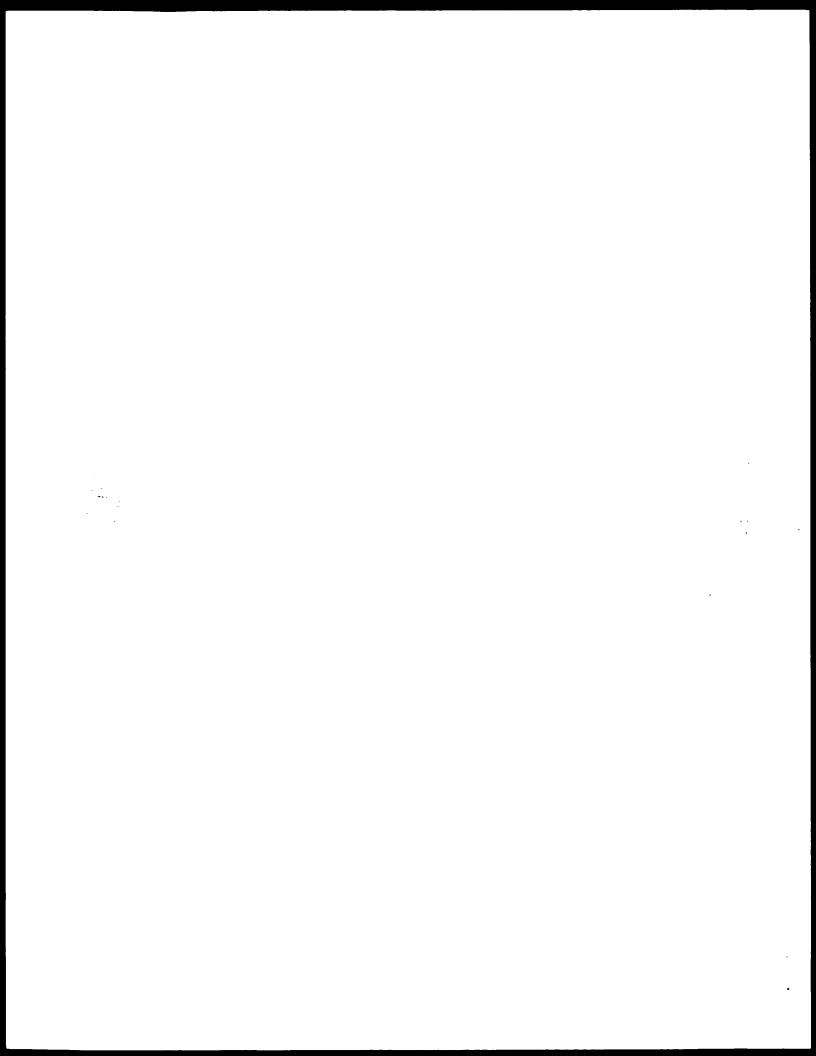
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ALIGNMENTS

AAQ41545 standard, DWA, 2994 AAU41545; KESULT 1 AAQ41545

24-AUG-1993 (Lirst entry)

Retineblastoma gene.

PB gene product; p5688 portion; cell cycle progression control; confided box, therapeutic methods; arrest; tomorphyrachis; repulation, physical at processes; blood cell product gamete products ss.

Homo sapiens SR-40 cell line.

Loration/Qualitiers

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retinoblasiona (RB) protein which may be used as part of a method of retirolling cell cycle progression which may be used in combination with therapeutic methods to arrest tumourjaenesis in combination cell cycle can be recersibly arrested in a convenient and safe manner. The protein is used in a compan, is relatively inexpensive and readily obtainable, and shows little or no toxic effects on healthy cells. It is also compatible with other methods and devices for requisiting perfects in processes of the brody such as blood cell prodo, and quante prodon. Bragments of the protein are soluble in low concus, of allycerol thus enhancing their value in
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                                                                   /note- "Rb protein"
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Sequence 2994 BP; 974 A; 618 C; 594 G; 808 I; 0 other;

2994 928 0 0		iaAlaAlaAlaSluFro 20 	inAspSerGlyProGlu 40 	coAspPheThrAlaLeu 60 HIIIIIIIIIIIIII EUGATTTTACTGCATTA 318	rpLeuThrTrpGluLys 80 	rstysClutcuTrpCly 100 	aeThrPheThrGluLeu 120
repath: Matches: Conservative; Mismatches: Indels: Gaps:	5 (1-2994)	ThrAlaAlaThrAlaAlaA) 	Procluciu <mark>aspProc</mark> iu61 	PheGluGluThrGluGluPr 	HISVATARGIUARGAIATE 	G yG yr yr 1eG args y 	AspLeuAspGluMetSerPE
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2659 ACTECEGGARANGTECCASAAAATAAATCAGATGEAALGEAACGAACGACGGGGGGGGGACAAAA 2718
                                                                           protein RB (see AAM62465). A new claimed polypopride is a fusion of all a transcription tactor (FF) comprising a LNA binding demain, and (ii) a transcription tactor (FF) comprising a LNA binding demain.

Suppression domain. As a containing a nucleic acid encoding the fusion protein, and (2) expression vectors containing such bNA. The fusion protein, particularly expressed from gene therapy vectors (cspecially adenovitually experise), is used to treat hyperproliterative conditions, specifically cancer (particularly of the bladder) or restenosis (after analogisaty), but also diabetic
                                            881 GlySerAspGluAlaAspGlySerLysHisLeuProGlyGluSerLysPheGluGluLys 900
                                                                                                                                                                      901 LeuAlaGluMetThrSerThrArqThrArqMetGlnLysGlnLysMetAsnAspSerMet 920
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             This nucleotide sequence includes a coding region for retinoblastoma
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    used to
                                                                                                                                                                                                                                                                                                                                                                                                                                                    Retinoblastoma protein RB: E2P; transcription factor; human;
bladder cancer, restendais, andioplasty, diabetic retinopathy;
thyroid hyperplasia; Crave's disease; psoilasis;
beniqui prostatic hyperfrophy; li Franment syndrome;
peripheral vascular disease; therapy; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 New fusion polypeptide of, e.g. transcription factor—use treat, e.g. hyper-proliferative disease such as cancer and restenosis
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                                                                                                                                                                                                                                     921 AspthrserAsniyscluGluLys 928
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                                                                                                                                                                                                                                                                                                                              AAV40004 standard; DNA; 2994 BP.
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                                                                                                                                                                                                                                                                                                                                                                                                                        Retinoblastoma protein RB.
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relinopathy, thyroid hyperplasia, Grave's disease, psoriasis, benian prostatic hypertrophy, Li-Fraumeni syndrome and peripheral cascular disease. Tissue specific expression of P2P-BH fissions is provided. The fusion proteins are more effective in repressing transcription of the P2P promoter than 8b alone and eager cell-cycle.

Sequence 2994 BP; 974 A; 618 C; 593 G; 809 T; 0 other; 928 Conservative: Mismatches: Matches: indels: ongth Gaps: 26-459A 2 (1-928) x AAV40004 (1-2994) arrest in a variety of cells. 100 00% 100 00% 4797.00 100.00% Percent Similarity: Best Local Similarity: Aliquatet Scores: Junery Match: ž

139 ATGROUNGAAAACCCCCCCAAAAACGGCCNINAINGCHINGHINGHINGHINGHINGGAAGCC 198 MetProProLysThrProArqLysThrAlaAlaThrAlaAlaAlaAlaAlaAlaAlaAlaGluPro 20

2) ProAlaProProProProProProProGluGluAspProGluGlnAspSerGlyProGlu 40

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259 GACCTGCCTCTCGCCTCGCCTTGAGTTGAAGAAACAGAAGAACCTGATTTTACTGCATTA 318 41 AspleadroleuValArgleuGluPheGluGluThrGluGluProAspPheThrAlaLeu

61 CysGlnf.ysLeuLysIleProAspHisValArqGluArqAlaTrpLeuThrTrpGluLys 80

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121 @lnLysAsn1leGl.IleSerValHisLysFhePheAsnLeuLeuLysGluIleAspThr 140 439 CAGAAAAACATAGAAATCAGTGTGCATAAATTCTTTAACTTACTAAAAGAAATTGATACC 141 SerThrLysValAspAsnAlaMetSerArgLeuLeuLysLysTyrAspValLeuPheAla 160 555 ASTACCAAAGTTGATAATGCTATGTAAGACTGTTGAAGAAGTATGATGTATTGTTTGCA

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1 AlaLys31yGluValLeuGloMetGluAspAspLeuValileSerPheGloLeuMetLeu

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221 CysVallouAspTyrPhollolysLouSorProProMotLouLouGysCluProTyrLys 240

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251 AlaArgiieAlaLysGlnLeuGlnAsnAspThrArgileIleGluValLeuCysLysGlu 280

1999 CGTGTAAATTCTACTGCAAATGCAGAGAGACAACAAGCTCAGGCTTCAAGAAA. 2658 6.3 401 lleSerfyrPheAsnAsaCysThrValAsnProtysGluSerfleLeutysArqValLys 420 421 AspileGlyTyrilePheLysGluLysPheAlaLysAlaValGlyGlnGlyCysValGlu 440 461 LeurysSerGluGluGluArgLeuSerTleGlnAsnPheSerTysLeuLeuAsnAspAsn 480 621 ArgValAsnSerThrAlaAsnAlaGluThrGlnAlaThrSerAlaPheGluThrGluLys 640 919 GTACGATAGCAAAAACAACTAGAAAATGATACAAGAATIAITGAAGTICTCTGTAAAAAA 978 301 AppSerLeuGlyLeuValThrSerAsnGlyLeuProGluValGluAsnLeuSerLysAru 561 JandalaTipladSetAspSetProjanPleAspJanijelysGinSetLysAspArg3Di 1099 TACGAAGAAATTTATCITAAAAATAAAGATCTAGAIGCAAGATTATTTTTGGATGAT 381 ThrileGinGinLeuMetMetHeLeuAsnSerAlaSerAspGinProSerGluAsnLeu 481 IlePheHisMetSerLeuLeuAlaCysAlaLenGluValValWalAlaThrTyrSerAru HELLER CTISCATOSCICICASATICACCITIALIGACIAAACAALCAAASSA CSACAA 581 ClyproThrAspHisLeuGluSerAlaCysProLeuAsnLeuProLeuGlnAsnAsnHis 281 HiscladysAsnileAspGlaVallysAsnValTyrPhetysAsnPbelleProPheMet 361 AsnLeuAspGluGluValAsnValIleProProHisThrProValArgThrValMetAsn 441 IleC!ySerCinArgTyriysLeuClyValArgLeuFyrTyrArgValMetGluSerMet 1519 CTTTAAATCAGAAGAAGGATTATCCATTCAAAATTTTAGCAAACTTGTGAATGACAA 541 AsnLeuThrArgGluMetIleLysHisLeuGluArgCysGluHisArgIleMetGluSer .759 AACTITGACAAGAAATIGATAAAAGATTTAGAAGGATGIGAACATGGAALCA FGGAALCO ThrAlaAlaAspMetTyrLeuSerProValArqSerFroLysLysLysCySerThrThr 341 LysThricuGinThrAspSerileAspSerPheGluThrGlnArgThrProArgiysSer SerThrSerGlnAsnleuAspSerGlyThrAspLeuSerPheProTrp11eLeuAsnVal 521 LeuAsmieuLysAlaPheAspPheTyriysValileGlaSerPhelletysAlaGluGly 501 х . a QQ qq qq φ ď g 3 ó QΫ́ ô õ ò δ $\ddot{\circ}$ ò qq ò ò

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RM gene; human; refinoblastoma gene; mutation detection; immunoscreening; refinoblastoma diagnosis; hereditary refinoblastoma; secondary cancer;
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The invention relates to a method of detecting a ministed rotinoblastomatimes in the first mannals comprising hybridizing an isolated detecting wild-type RB (wirk) cPNA probe to a cell sample and detecting a mutated RB uncleis acid. The method is useful as a diagnostic trool for diagnosting retinoblastoma. RH culNA or genome INA are preferably used as probes to determine the defect region of the method contribution.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           length polymorphism analysis to determine the diseased allele, cloned RB cDNA can be used to generate specific anti-RB protein (anti-ppRBJ10)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                cancer whether or not connected with rethnoblastoms. The method is also used in the suppression of tumouriquesis where the absent RB protein ppRBIIO will be provided through the molecular induction and que
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  antibodics which are ascful for immonoscreening of tissue biopsy. The diagnostic method is particularly intended for use in sereening families with a history of hereditary retinoblastoma and for sereening
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          ransplanting of the RB cDNA to the individual in need of ppRB110.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           their children. It may also be used in prophylactic and postnatal screening and for the prediction of the development of promotary
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                cancer, such as, osteosarcoma, tibrosarcoma, qlioblastoma, breast
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       this sequence represents the Wild type human retinoblastoma gene.
OsteoSarcoma; fibrosarcoma; qlioblastoma; breast career; tamourigenesis suppression; ss.
                                                                                                                                                                                                                                                                                                                                                                                                         Detecting retinoblasions gene cancer in mammais
                                                                                                                                                                                                                                                                                                                                                                                                                                                  Example 6; Fig 7; 34pp; English.
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                                                                                                                                                                                                                                                                    (REGC ) UNIV CALIFORNIA.
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                                                         Homo sapiens.
                                                                                                                                                                                                               15-OCT-1987;
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                                                                                              US5998134-A.
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Conservative: Mismutches: Matches: Length: 100.00**%** 100.00**%** 4797.00 100.00% Percent Similarity: Best Local Similarity: Ouery Match:

Sequence 2994 BP; 974 A; 618 C; 594 G; ROB T; 0 other;

Alignment Scores:

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Recombinant adenovital vectors useful for gene therapy of cancer,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Human; pll0 88; retinoblastoma; tumour suppressor; gene therapy;
                                                                                                                                                                                                          Human pll0-RB retinoblastoma tumour suppressor encoding cDNA.
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The present invention describes a composition comprising a recombinant adenovirus expression vector, where the vector has an insert of exogenous DNA comprising a gene encoding a horizon protein and adenovirus BNA in which all of the roaling sequences of Ela, Elb, and protein IX, and part of Ela are deleted. The vectors are useful in gene theory treatment of cancer, especially for treating p53 deficient thmours. The vector enables safer and more efficient enumeurs. The present sequence encodes homen p110 KB retinolastoms tumour suppressor which can be used as the foreign gene in the above
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                                                                                                            2059 C'ATTSAAAFCTACCTCTTTCACTGTTTALAAAAAASTSTAFCSSCLASCCTACTC
                                                                                       641 ProLeuLysSerThrSerLeuSerLeuPheTyrLycLysValTyrArqfeuAlaTyrLeu
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comprising a deletion in the protein IX gene and a gene encoding a foreign protein. This vector can be used in gene therapy, particularly to introduce tumour suppressor genes into cancerous rells. Genes which may
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Recombinant ademovinus expression vector comprising a partial or total deletion of a protein IX BNA and a gene encoding a foreign protein e.g. suicide protein, useful for inhibiting or reducing the proliferation of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  be used include p54, thymidine kinase and retinoblastema tumour suppressor qene (Rb). The present sequence is the retinoblastema tumour
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             FBF POLICY CONTRACTOR CONTRACTOR I CONTRACTOR CANDACTAR CANDACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR CONTRACTOR 
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                                                                     Retinoblastoma: tumour suppressor profein; RD; p53, ca
adenozitak zector; gene therapy; thymidine kinase; ds.
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   Retinoblastoma tumour suppressor gene.
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                 141 SerThrLysValAspAsnAlaMetSerArqLeuLeuLysLysTyrAspValLeutheAla 160
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Refineblastoma; PB; tumour suppressor protein; pll088; p53; gene therapy; cytestair artityroid, artipscriat(), identrial protein IX; psortasis; chirolital hyperplasia; cruck's disease, hebatocellular carcinoma, neoplasm; beatan prostalic figerticaphy. If Frammeni syndromes sickle cell anomala; Tay Sacha disease; leikherii, lymphoma, identrials elika anomala;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             The present cDNA sequence encodes retinoblastoma (RR) tumour suppressor protein, designated as p110RB.
The invention relates to a recombinant adenovirus expression vector characterised by the partial or rotal delation of the adenoviral protein
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                                                                  2659 ACHTOTICAGAAGTTGCAGAAAATAAATCAGAIGGTAAGGAGGGAGGGTGIGGTGAAA 2278
                                                                                                                     2599 ACACCAACAAAAATGACTCCAAGATCAAGAATGTTAGTATGAATTGGTGAATGATTGGGG 2558
                            841 ThrserGluLysPhcClnLysllcAsnClnMctValCysAsnScrAspArqValLcuLys 860
                                                                                                     861 ArqSerAlaGluGlySerAsnProProLysProLeuLysLysLeuArqFheAspIleGlu 880
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p11088"
                                                                                                                                                                        881 ClySerAspGluAlaAspGlySerLysHisLeuProGlyGluSerLysPheGlnGlnLys
                                                                                                                                                                                          901 LeuAlaGluMetThrSerThrArgThrArgMetGlnLysGlnLysMetAsnAspSerMet
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Retinoblastoma tumour suppressor protein, pl10RB cDNA.
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lx bwa bequinded at nucleotides 457 or 460 and ending at 4020-4050, and having a gene encoding a foreign protein such as tumour suppressor for exercise the first state is used for screening tumour suppressor genes useful in gene therapy. The vector is particularly useful for freating or reducing hyperproliterative cell disorders such as thyroid hyperphasia, of answer, psorlasis, become as thyroid hyperphasia, of answer, psorlasis, become prostatic byperformer, encodes specifically hepdrocellular carrinoma, neoplasms, lowkaemids, lymphomas, etc. to highly thomore proliteration or to amelicate particular related pathology such as sixthe early analysis of any sactic for and lay-sacks disease. The vector is also useful for the safe recombinant production of diagnostic and therapeutic polypoptides and proteins.

Sequence 2995 BP; 975 A; 618 C; 593 G; 809 T; 0 other; 8999988888888**%**&

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The present invention describes a recombinant adenovirus expression and a state conditions a partial or total deletion of a protein IX DNA and a state chouling a foreign protein. The recombinant admonstrate vector can have expostate activity and be used in gene therapy. The recombinant adenovirus expression vector is particularly useful for treating or small end profileration of a tumour, e.g. non-small cell lung cancer, small cell lung cancer, small cell lung cancer, small cell lung cancer, the action of a tumour, adopted a carcinoma, melanoma, retinoblastoma, breast tumour, adopted acrinoma, sarroma prostate tumour, bladder tumour, tumour of the reticuloridation as arroma tissues, whim's tumour, astrocytoma, gliopolastoma, neuroblastoma, ovarian catchinoma, ostwosarcoma or retail ancer: The present sequence encodes the retinoblastoma tumour suppressor protein pilo RB, which is
                                                                        Retinoblastoma; tumour suppressor protein, pl10-RB; cell cycle; p53; Pb; mitosin; cell death; adenovira! protein IX, quic theisp; sjusitati; adenovirus expression vector; tumour; non small cell luna cancer;
                                                                                                                             small cell lugg cancer, hepatocarchioma, hepatocellular carchioma:
melanoma; retinoblastoma; colorectal carchioma; sarcoma; Wilm's timour;
astrocytoma; glioblastoma; neuroblastoma; cvarian carchioma;
                                                                                                                                                                                                                                                                                                                          /product= "retinoblastoma tumour suppressor protein"
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                                      Retinoblasfoma fumour suppressor profein pl10-RB encoding (DNA)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      given in the exemplification of the present invention.
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                                                                                                                                  inhibiting cellular proliferation, particularly cancer
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Mismatches:
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P-PSDB; AAW69364.
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                                                           621 ArqValAsnSerThrAlaAsnAlaGluthrGlhAlathrSerAlatheGluthrGlutys 640
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suppressor proteins which can be used for treating diseases characterised
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                                                                                                                                                                                                                                                          Minimal promoter, tetracycline responsive expression vector; TREV; representivitional transportive from domain; True; tetracycline repressor protein, TREV, tetracycline operator; from a stable cell line; protein production; stable cell line; protein cancer; ss.
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41 AsptwuProteuValArgteuGluPheGluGluThrGluGluProAspPheThrAlaieu 60

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127 GACCHGCHCHCGHCAGGCH1GAGTFFGAAGAAACAGAAGCHGATTFFFAJFGFAFFA 185
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hEST2: telomerase, catalytic subunit; reverse franscriptuse; life span:
retinobiastoma; p54; tumour suppressor; inhibitor; afternosclerosis;
proliferation; immortal; tumour therapy; macular degeneration; activator;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     The invention concerns methods and readents for extending the life span, e.g. the number of mitofic divisions, of a cell. The method felles on
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                                                                                                        2647. GGATCAGATGAAAGAGAGGAAGTAAAACALCTCC.AAAGAGAGTCAAA111. AAFAYAAA 2706.
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                                                      801 SlyGlyAssileTyrileSerProLeuLysSerProTyrLysIleCetSloSlyLeafto 820
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Human retinoblastoma gene.
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Treat conditions related to (premature) againg, e.g. macular degeneration and arteriosclerosis. The cells can also be used to replace tumour cell lines in vitro and for studies of biochemical and physiological aspects of growth and differentiation. Long lived (immortal) cells could also be or use in the production of normal or genetically engineered artication of a telomerase activity and inhibition of one or both of a netinoblastoms (Rb)/INM4 pathway or a p53 pathway. Physphorylation of Rb by eyeller Eggenbut Pfances. ARI and eBMC releases the oills into the division cycle. Binding of TNK4 family members, e.g. the tumour suppressor planka, inhibits kinase activity and results in growth arrest pe handless can sale-tively and results in growth arrest pe handless can sale-tively and results in market and the service of the function and the p53 tumour suppressor and can also be used in the merhods. Other melecules which can be used in the defined to particular, a cdk4 mutant is one which differs that are more its about a cold market by a differs of the methods to the methods of the market by the and, and the based differs that are more its about a self-mutant is one which differs that are more in about any virus B7 protein, or other subsequently of use in pharmaceutical and cosmetic preparations used to And issues constructs of viral oncoprotein which bypasses Bh and/or p53. Antiseuse constructs of the Rb and plfinK4a genes may also be used. The methods are useful for increasing the proliferative capacity of cells, the cells are that echnology products.

Sequence 4839 BP: 1534 A: 902 C: 880 G: 1523 I; 0 other;

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1038 AATICITICGGACTIGIAACAICTAAIGGACTICCAGAGGIIGAAAAICIIICIAAACGA 1097
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                                   381 ThrileGinGinLeuMetMetHieLeuAsnSerAiaSerAspGinProSerGiuAsnLeu 400
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678 ATAICTACIGAAAIAAAIICIGGAIIGGIGOIAAAAGIIICCIIGGAICACAIIIIIAIIA 747
                                                                                                                   221 C,sValle_AspTyrPhellel,sLeuSerProFroMetLeuLeuLysGluProTyrLys 240
                                                                                                                                          241 Thr AlaVall1cPtoIlcAshSlyScrProArgThrProArgArgSlyClnAsaArgScr 260
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                                    BIB PILGCALOD TO GAGALICACOTILALIDA COLLA TRABACA ATCA A A GAGGGAGA A 1877
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561 LeuAlafrplæuSerAspSerProLeuPheAspLeuIleLysGInSerLysAspArqGlu 580
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designated Rb. Androgen receptor co-activator proteins from the present invention can be used in a regenied assays to identify candidate pharmaceutical molecules for the ability to promote on inhibit the interaction of androgen receptors and androgen responsive elements to modulate androgen estivity. The identification and characterisation of androgen receptors such as those of the invention will
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           lacilitate the development of screening assays to evaluate the potential
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Novel androgen receptor associated proteins used to detect androgenic or antiandrogenic activity in screening assays for candidate pharmaceutical molecules which promote or inhibit the activity.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Ruman; androgen receptor coactivator; ARA54; ARA24; detection;
Rb; androgenic; antiandrogenic; identification; prostate cancer; 88.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               The present sequence encodes a human androgen receptor coactivator
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                                                                                                                                                                                            Human androgen receptor coactivator Rb encoding cDNA SEQ ID No.7.
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                                                                                                                                                                                                                                                                                                                                                                       Znote- "androgen receptor coactivator"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            efficacy of drugs in the treatment of prostate cancer.
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                                                                                                                                                                                                                                                                                                          Location/Qualitiers
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                              2898 GALAMMICAAACAAMMAAAAA 2921
921 AspThrSerAsaLys71s71sLys 928
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                                                                                               AA288444 standard; cDNA; 4839
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The present invention describes a method (M) for screening for an anti-neoplastic agent. The method involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, determining a change in expression of at least one quee (1) of a signature gene set, where (1) comprises a sequence (S) selected from R47 sequences (given in Anish 664 to AMEZOHO), or is at least 5% identical to (S). Where a change in expression is indicative of anti-neoplastic activity and can be used in gene therapy. M can be used for producing a product which is the data collected with respect to the anti-neoplastic agent as a structure and/or properties of the agent. M can be used to remain a structure and/or properties of the agent. M can be used to the static treatment of cancer such as colon, breast, stomach, lune, thyroid,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               oesophageal, ovarian, Kidney, prostate or pancrealic canrer, adenocarcinoma, carcinoma, clear cell cancer, infiltratina ductal cancer.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               chemical agent to be tested for anti-neoplastic activity, and determining a change in expression of a gene of a signature gene set
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                                                                                                                                                                                                                                tumour protein. The gene can be used in a movel method involving a recombinant adenovitius expression vector to treat discusses associated with the ausence of the Tsq or the presence of a mutated TSG, e.g. many forms of carcinoma, sickle cell anaemia of Tay Sach's
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                                                                                                     Adenoviral vector with deletion of viral protein IX contains foreign gene - esp. encoding tumour suppressor protein for gene therapy of tumours, reduces contamination by wild type adenovirus
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By installing a working CSC, safe and specific treatment and
prophylaxis can be given to cancer patients.
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                                                                  AAU04713 standard: cDNA; 2994 BP.
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2539 GGAGGGAACAICIAIAIIICACCCCIGAAGAGICCAIAIAAAAIIICAGAAGAITITGAAAAA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        CDNA encoding a retinoblastoma protein designated ppRB-110 or pliv-RB.
                                                                                                                                                                                                                                                                                                  861 ArgSerAlaGluGlySerAsnProProLysPreLeuhysLysLeuArgPheAsplleGlu 883
                                                                                                                                                                                                                                                                                                                                                                                                                      881 GlySerAspCluAlaAspClySerLysHisLouProClyCluSerLysPheGlnGlnlys 900
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designated ppRB 110 or p110.88. The protein is used in a method for inhibit ing proliferation of pathologically proliferation genelis acking rendequency tunctronal retinoblastoma protein. The method comprises contacting the cells with a polypeptide camplising a 56 KD forminal transment of retinoblastoma protein. The method is useful to treating cancers, especially retinoblastoma or secondary ostrosarroma, breast cancer, small-cell lung cancer or fibrosarcoma.
                                                                                                                                                                                               The present sequence encodes a hyman retinoblastoma (PP) protein
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Sequence 2995 BP; 975 A; 618 C; 593 G; 809 1; 0 other;

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Search completed: January 18, 2003, 08:34:20 Job time : 432.07 secs

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nucleic search, using sw model M michelo

January 16, 2003, 15:20:17 ; Scarch time 435.71 Seconds (without alignments) 17531.794 Million cell updates/sec HID OTH

US 09-026 459A 30 3392 inthe: Perfect score:

1 GCCATCATCOATTIFACTCC......AAATCACCATTATTCATACT 3392 Sequence:

IDENTITY_NUC Gapop 10.0 , Gapext 1.0 Seoring table:

2185249 seqs, 1125949159 residues Sear ched:

Foral number of hits satistying chosen parameters:

Minimum DB seq length: 0 Maximum DB seq length: 2000000000

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Prod. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

	Description	Modified retinobla	Modified retinobla	Modified retinobla	DNA sequence of the	Human retinoblasto	Human androgen rec	Breast cancer rela	Human retinoblasto	Human retinoblasto
	15	AAV5844.2	AAV58441	AAV58440	AAV54990	AAA29391	AAZ88444	ABL62873	AAU705 16	AAX04501
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Modified retinobla	Human retinoblasto	Human retinoblasto	Modified retinobla	Probe for retinobl	Modified retinebla	Modified retinobla	Modified retinobla	DNA sequence of th	Ketinoblastoma 94k	Modilied retinobla	Modified retinobla	Modified retinobla	Modified retinobla	CDNA of human reti	Modilied retinobla	Camer supressing	Retitooblastoma qen	Refinoblastoma pro	Wild type human re-	Homan pilo RB reti	CINA encoding a re-	Retinoblastoma tum	Refinoblastoma tum	Retinoblastoma tum	Retinoblastoma tum	Human Rb110 cDNA.	Buman retinoblasto	DNA of human retin	Antiscuse sequence	Direct tandem repe-	Construct part AS		Counting Continue	Retinoblastoma pro	Retinoblastoma pro
AAV58452	AAN8 369	ABK86079	AAV5844 1	AAN81261	AAV58444	AAV58446	AAV58447	AAV54931	AAQ72690	AAV58445	AAV58451	AAVSH450	AAV58448	AAN90485	AAV58449	AAQ04713	AAQ41545	AAV4 0004	AA240287	AAX50450	AAX007 47	AAH25755	AAD04474	ABL50904	AAQ90059	AAQ86 498	AAX04502	AAN90490	AA1 62 490	AAT62391	AATLECT	AATCESC	AAT 62 P. G.	AAT01542	AAT01541
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ALIGNMENTS

RESULT 1

AAV56442 standard, DNA, 3392 HP. 02-DEC-1998 (first entry) AAV58442; AAV58442

Modified retinoblastoma tumour suppressor gene.

Modified retinolastome tempor suppressor; RTSP protein; camper therapy; of did profileration inhibitor, ss.

Homo sapiens.

Location/qualitiers 7..2641 /*taq- a

W09837091-A2

27 - AUG - 1998.

98WO-US04041. 19-FEB-1998; (BAYU) BAYLOR COLLEGE MEDICINE. (TEXA) UNIV TEXAS SYSTEM.

97US-0038118.

20-FEB-1997;

Benedict WF, Ru S, Xu H, Zhou Y:

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                                                                                                                                                                                                                                                                                    proliferation, particularly cancers, the RISEs have a broader spectrum of activity than wild type RISEs.
                                                                                                                                                                                                                                                       The RISEs
                                                                                                                                                                                                                   problem (KTSP) of the invention. The proteins can be used for inhibiting cellular profileration, when commissions with a FS protein. The RTSR can be used for treating diseases characterised by abnormal cellular
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    AGAGCI IGGTTAACTTGGGAGAAGTTTGATGTGTGTGGAGTATTGGGAGGTTATATT 120
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                                                                                                                                                                                                      This sequence encodes a modified retinoblastoma tumour suppressor
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                                                                                                                                                                                                                                                                                                                                                                                                                           100.0%; Score 3392; DB 19; Length 3392;
100.0%; Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Indels
                                                                                                                                                                                                                                                                                                                                                                             Sequence 3492 BP; 1137 A; 614 C; 607 G; 1034 T; 0 other;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                             0; Mismatches
                                                                                                                                                  Claim 22; Page 150 155; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Matches 3392; Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                                      Similarity
WP1: 1998-480788,41
                            P PSDB: AAW69366
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781 GAGGITGAAAATCITTGIAAACGATACGAAGAAATTTATCITAAAAAITAAAGATCITAGAT 840
                                                                      841 GCANSALTATITITAGAICATGAIAAAGITTICAGASIGALIGIAIAGAGAGITTIGAA 900
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                                                                                                                 841 GCAAGATTATTTTGALGATGATAAAACTGTTGAGACTGATTGTATAGACAGTTTTGAA 900
                                                                                                                                                      901 ACACAGAGAACACCACGAAAAAAGTAACCTTGATGAAGAGGTGAATGTAATTCCTCCACAC 960
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<u> </u>	186.1	CACOCAGA FILLE FIL
S 3	1921	GAACTCATGAGACAGACATTTGGACGAAATTATGATGTGTCCALGTATGGGGAGATATGC 1980
	1981 1881	AAACHGAAGAATAFACACCTTAAATTCAAAATCATGTAACAGCATACAGAAGCTCTCCT 2040
학 중	2041	CATOCTOTICAGGAGALICAAACGIGITIGAICAAAGAAGAGAGATAIGTATT 2100
\$ £	2101	ATAGTATTCTATAACTCGGTCTTCATGCAGAGTCTGAAACAAATATTTTGCAGTATGCT 2160
ਤੋਂ ਤੋਂ	2161	PYTAYYADDOOCTAYULIGEGAATAGOLGAATTGCTGGAAGGCTTAGAAGTTT 2220 HITTITTITTITTITTITTITTITTITTITTITTITTITT
A 2	2221	PETABITEACOCTIACRIA LEGIGOAGIAGA CATATATTEACOCTGAAGACTCCA 2280 ELLELLELLELLELLELLELLELLELLELLELLELLELL
5 g	2281 2281	TATAAAATTTCAGAAGGTCTGCCAACAACAAAAATGACTCCAAGATCTTA 2340 HILLIIIIIIIIIIII TATAAAATTCAGAAGGTCTGCAACACAACAAAAATGACTCCAAGATCAAGAATCTTA 2340
\$ £	2441	TA 240 240
<u>}</u> 4	2401	INTRACACHONGOCOTONNICAAAAGAACHONIGAAGGAACHONIACHAAACHOOLG 2460
\$ £	2461	AAAAAATTAGOTTTGATATTGAAGGATCAGAGAGGGGAGGTGAAGTAAAGATCTCCCA 2520
	2521	-BAGABI CHAAATI LAACABAAACI GOCABAAA BACTI CHACI CHAAGAAGAAT GCAA 2580
§ 9	1857	ICAG 264 CAG 264
숙물	26.41	TGTGTACACGTCTGGATTCATGGTCTCACACAGAGGGACTGTAT 270 LLTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT
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5 8	2761 2761	AAATGERGAALIGEAALIGEREATEGERAAGGGACITGAAATGELAGEGATGTT. 2820 FEELEELEELEELEELEELEELEGGGGACTGGAAAGGGACTGGAATGELAGGGATGTT 2820 AAALGEGAGATGGGATGGATGGTAAGGGACTGAAATGELAGGGATGTT 2820
	2821 2821	ATTITATA'AAGATTGAAAATGTTGTAAATGCTGCCATTTAAAAAGTTGTAGCAGATTG 2880
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17	2.44 [GAGLOCICATAACCAGGCIGICICACITICCTICTTTGTACCATATAGGTGAT 3000

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This sequence encodes a modified retinoblastoma tumour suppressor protein (Risk) of the invention. The proteins can be used for inbibiting
                                                                                                                                                                                                                                                                                                                                                                                                                                           Modified retinoblasfound tunnout suppressor, KLSP profein; cancer therapy;
                                                                           3001 GTTGCTCTTGTTTTATTAATTTATATGTATTTTTTTTAATTTTAACTGAACACCTT 3060
                                                                                                       3181 TACACATTAGATTTTATTTTACTATTGGAAICTGATATACTGTGTGTGTTTTAJAAAA
                                                                                                                                                  3061 AGAAAATGTGTATCTATCTTGCAAATGCAATTTGATTGACTGGCGTTCACGAAAT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Ketinoblastoma suppressor protein with N terminal modification inhibiting couldbr proliferation, particularly cancor
                                                                                                                                                                                                                                                                                                                                                                                                                      Modified retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                         3361 ACTTATGTTTTTAAATGAGGATTATTGATAGT 4392
                                                                                                                                                                                                                                                                               3361 ACTIATGITITIAAATGAGGATTATTGATAGT 3392
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Claim 22; Page 142-147; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                     cellular proliferation inhibitor; ss.
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                                                                                                                                                                                                                                                                                                                                                       AAV58441 standard; DNA; 3455 BP.
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when coadministered with a p53 protein.
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clar proliferation, when coadministered with a p53 protein. The RTSPs be used for treating diseases characterised by abnormal cellular iferation, particularly cancers. The RTSPs have a broader spectrum of vity than wild type RTSPs.	h 3455	TAAAGATACCAGATCATGAGAGAGAGAGAGGTGG 69 	PCAAAA TCAAAA	3ATGTC 111111 3ATGTC	TARAAATCARIGTOOALAAATCITTAACHACIA 249 	SAAGAAGTAT 30 	ATATTIGACA 36 ATATTTGACA 43	AGTITUTIGG 42 	GGTGATTTCA 4 	TGCIC 5	WOCATATAAAACACETTATAPOPA11AAFBBTLCACTPCBAACACCABBCBA 609 FELLHTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	FTGAA 6	AAAAT 7	TIGAA 7	SATTA 8	AGAGA 9 AGAGA 9	JGANGAGGTGAATGTAATTCCTCCACACACTCCAGTT 969
collidar proliferation, we can be used for treating proliferation, particular activity than wild type R sequence 4455 Rp; 1153 A;	datch 99.7 cal Similarity 100.	GATTTTACIGCATTAIGICA	ITAACTIGGGAGAAAGTTTC 	AAGGAACTGTGGGGAATCTG	ACTITIACIGAGCTACAGAA 	AAAGAAATIGATACCAGTAC 	GALGIALTGITTGCACTCTT GALGIALTGITTGCACTCTT GALGIALTGTTTGCACTCTT	CAACCCAGCAGTTCGATATC) ATCACATITITATIAGCTAA 	ĕ ĕ	AAAGA AAAGA	GG FPA GGTCA	GITCI	TTTAT/	AA1C1 21111 AATCT		ACACO 11111
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                                                                                970 AGGACTGTTATGAACACTATGCAACAATTAATGATGTTFFFAATFFCAGGAAGTGAA 1029
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	3192	41.3.3 GESTIATOTATOTISCAAATGCAATTIGATTGACTGCCCATTGACAAAATTATCCTGAA	â
	3129	8070 GFCTPATCTTCCTCCAAATGCAAATTGATTGACTGCCCATTCACCAAAATTATCCTGAA	5
	3069	4010 TOTTTTTALTAALTTALATGTALATTTTTAALTTAACATGAACGCGTTAGAAAATGT TTTTTTTTTTTTTT	5 G
	3009	2950 TAACCCAGGCHELCTACTTGCCTCTTTTTTTTTTTTTTTTTTTTTTTTTTTT	55
	3012	2930 CYAAACTAAAATTGCTGTTTTATGGATAGTAAGAATGGCCCTAGAGTGGGAGTCCTGA 2947 	5 3
	2889	2830 AGAITGAAAALCTIGIGIAAALCCTGCCALFIAAAAAGTTCFAGCAGATTGFTTGCTGTTTCTTTGTTTGCTGTTTTTTTTTT	5 3
	2829	2770 GAFGTANTROCCIGALICCTAAGCCACTICAAALGITAGICATIGITANTAAACAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	5 3
	2769 2832	2710 ABSTICTUTITATOROCACATITAATATCTICAGCICTITITGTGGATATAAAAIGIGGA HI HILLIHIHIHIHIHIHIHIHIHIHIHIHIHIHIHIH	5 6
	2709	2650 GGATACHGIGTACAPHGIGALICALIGICHGICHCACACAGAIGIGACHGIAIAETTGCC TELLITITITITITITITITITITITITITITITITITIT	5 g
	2649	2590 ALGAALGALGGALGGALGGALGGAAGAGAGAGAGAGAGA	5 g
	2589	25.40 AAATTTCAGTAGAAATTGGCAGAAATGACTTCTAGTCGAATGCGAATGCGAAAAGCAGAAA 	5 €
-	2529	2470 CONTINGALATICAAGGATGAGAAGAAGAAGTAAAGATAAAGATGGGAGAGAGGG 1111111111	<u>}</u>
	2469	2410 MAY OLG FOR LOAAAAAATOO IGAAGGAAGCAAACCIDCIAAADCACTGAAAAACTA THE THE THE THE THE THE THE THE THE THE	5 3
	2409	2.450. REFRATERATORIRACTTORIRAGANGTTCCRRANATAANTCRRATGGTATGTAACACCTTTTTTTTTTTTTTTTTTTTT	\$ £
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	2229	2179 POPOCTAVOTTGFONGCAANACCTGACATEGETGAAGGGGTTAGAAGTTFGCTAGTAGA 	5 3
	2232	2110 TATAACHOOTOTTOATOPAGAGACAAAATTTTTTTTTTTTTTTTTTTTTTTTTTTTT	5 3
	2109	ZUSU PARTARAN I CAAACOIGI HIIGAFAAAQAAGGGGIAIGAII CIAHAAGAATG 	5 £

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protein (RTSP) of the invention. The profeins can be used for inhibiting cellular proliferation, when coadministered with a p54 protein. The RISPs can be used for treating diseases characterised by abnormal collular proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Modified retinoblastoma tumour suppressor; RTSP profein; cancer therapy;
                 3130 CICTICICCAAAAAIGGATAITAITAGAAAAITAGAAAAAITATAATITTAGAAATIA
                                                           3190 GAITTTATTTTACTATTGGAATCTGATATACTGTGTGTTTTTTATAAATTTTGCTTT 3249
                                                                           3250 TAATTAAATAAAAGCTGGAAGCAAAGTATAACCATATGATACTATGTATACTACTACTGAAACA 4409
                                                                                                                                                                               3310 GATITCALACTICAGAALGFAAAGAACHTANIGALLATITLULLOALOGAACTTATGTT 3369
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    This sequence encodes a modified retinoblastoma fumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Query Match 99.7%; Score 448; DB 19; Length 455;
Hest Local Similarity 100.0%; Pred. No. 0;
Matches 3883; Conservative 0; Mismatches 0; Indels 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Retinoblastoma suppressor protein with N-terminal modification inhibiting cellular proliferation, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 3555 BP; 1171 A; 684 C; 654 G; 1047 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                      Modified retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Disclosure, Page 121-126; 249pp; Enqlish.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  cellular proliteration inhibitor; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Zhou Y;
                                                                                                                                                                                                                                                         3370 ITTAAATGAGGATTATTGATAGT 3392
                                                                                                                                                                                                                                                                                                                                                AAV58440 standard; DNA; 3555 BP.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         (BAYU ) BAYLOR COLLEGE MEDICINE.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Benedict WF, Ha S, Xa H,
                                                                                                                                                                                                                                                                                                                                                                                                        02 DEC 1998 (first entry)
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1689 2151 1090 CTGAAAAGAGTGAAGGATATAGGATACATCTTTAAAGGAAATTTGGTAAAGTGGGA 1149 1252 CTGAAAAGAGTGAAGGATATAGGATACATCTTTAAAGAGAATTTGGTAAAGTGTGGGA 14:3 1150 PAGGGFFGFGFFGFGAATFFGGAFGAGGGATAGAAACFFGGAGFFFGGCFFGFTGCGA 1209 1270 CITCIGAAIGACAATTITITCATAIGICTITAATGGGGGGGTCTIGAGGIIGIAATG 1329 1390 TGGATTCHGAALGIGCTTAATTTAAAAGCCTTTGATTTTACAAAGIGATGGAAGIIII 1445 1552 TGGATTCTGAATGTGCTTAATTTAAAAGCCTTTGALFFFFACAAAGTGATCGAAAGTIII 1611 1792 CTCCAGAATAATCACACTGCAGAGATATGTATCTTTCTCCTGTAAGATCTCCAAAGAAA 1851 1750 TTCCAGACCCAGAGGCATTGAAATGTAGGTGTCI CIGAGIGTTTTATAAAAAAGIGIAI 1809 1810 CGHTIAHTIIATETETHANIATATATATITHTGAACHETTETETETGAGCACTAGAA 1869 1930 ACAGACAGGCATTTGGACCAAATTATGATGTTGGTTGGATGTGGCATATGCAAAGTGAAG 1589 2050 CAGGAGACATTGAAACGTGTTTTGATCAAAGAAGAGGAGTATGATGATTGTATTATAGTALL? 2109 2110 TATAACTGGGGTGTGATGGAGAGTGAAAAGAATALTIGGAGIAFGCIICCAGGAGGG 2169 2272 TATAACTGGGTGTTGATGGAGAGTGAAAAQAAJATFTTGGAGTATGCTGGAGGAGG 2431 2170 CCCCCTACCTTGTCACCAAIACCTCACAIICCTCGAAGCCCTTACAAGTTTCCTAGTICA 2229 1330 GOCACATATAGCAGAAGTACATOTOAGAATOTTGATTGTGGAAGGAGATTTGT/PTTGGGA 1312 CAGGGTTGTGTGGAAITGGATGAGGATACAAAQTTGGAGITGGCIIGIATIACCAA 1450 ATCAAAGCAGAAGGCAACTTGACAAGAAAATGATAAAAACATTTAGAACGATGTGAACAT 1612 atgaaagaagaaagtigagaagagaaatgataaaagatttagaaggalgigaaga; 1570 TCAAAGGACCGAGAAGGACCAACTGATCACCTTGAATGTGCTCTGCTCTAATGTTGCT 1690 AAAGGTTCAACTACGCGTGTAAATTC1ACTGCAAATGCAGAGACACAAGGAACCTGAGCC 1870 TTAGAACATATCAGTGGTGTTTOCAGCACOCOCOSSAGAATCAGTACGAACTGATG 1210 GTAATGGAATCCATGCTTAAATGAGAAGAAGGATTATGCATTGAAAAIIIIAGGAAA 1990 AATATAGACCTIAAATICAAAATGATTGTAACAGGAIACAAGGAICTICCTCATGCTTT 2152 AATATAGAGGTTAAAATTGAAAATGATTGTAAGAGGATAGAAGGATGTTGGTGATGTT 2212 CAGGAGACATTCAAAAGTGTTTTGATGAAAAAAGAGGGTATGATTGTATTAIAGATT 엄 qq QQ a qq £ qq q Ś οy ŏ ò ò ŝ οy

3370 IIITAAAIGAGGAIIATIGAIAGI 3492

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2391	2289	2349	2409 2571	2469 2631	2529	2589 2751	2649	2709 2871	2769 2931	2829 2991	2889 3051	2949 3111	3009	3069 3231	3129 3291	3189 3351	3249	3309
CPPCCTACTTCTTTTTTTTTTTTTTTTTTTTTTTTTTTT	CCTTACGALICTIGAGGAAFALTIALITITITITITITITITITITITITITITITITIT	TCAGAAGGECTGCCAACAACAACAACAACACTCCAAGAATCAAGAATCTTAGTATCAATTTTTTTT	GGESAATCATECGGGACTTCTGAGAAGTTCCGGAAAATAAATCAGATGGTATGTAACAGC - - - - - - - - - - - - - - - - - - -	GAPYGEGEGTE AAAAGAAGEGCEGAAGGAAGCAACCCTAAACGACTGAAAAACTA 	COPTITICATATTCAMOSATCAGATGAMOCAGATGGAMOTAAACATGTGGGAGAGAGCCTTTTTTTTTTTTTTTTTTT	AAATTTCARCARAACTGGCAGAAATGCTTCTACTCGAACACGAATGCAAAAGGAGAAA 	A LOAA IGA FADOA FACOPAAACAADAAAGAAATGAAGAFICICAGGACOFIGOT TITTITITITITITITITITITITITITITITITITI	GRAPACTGTGTACACCTGTGBATTCATTGTCTCTCACAAGTGACTGTAACTTTCCCTTTCCCTTTTTTTT	ABBITCTGFTFAFGBOTACATTAATAFCFTCAGCTCTTTFGFGGATATAAAATGFGCA 	GATOPAATIGITTOODGICAATICCTAAGGNACTIGAAATGITAGITCATIGITATITTATAGA TIL TITTITTOTTITTITTITTITTITTITTITTITTITTITT	AGATTGAAAATGTTGTGTAAATGCTBGCATTTAAAAAGTTGTAGCAGATTGTTTGCTCTT 	CCAAAGTAAAATEGCTGFGCTTTATGGATAGTAAGAATGGCCCTAGAGTGGGAGTCCTGA 	TAACCAGGCCTGTCTGACTACTTTGCTACTTTGTAGCATATAGGTGAGCCTGTTTTTTTT	TGFTFTTATTAATTTATATGTATATTTTTAATTTTAACATGAACACGGTTAGAAAATGT 	GPCTATCTATCTFCCAAATGCAAATTGATTGACTGCCATTCACCAAATTATGCTGAA 	CTCTTCTTCTAAAAA DOATATTATAGAAATTAGAAAAAATTACTAATTTTACACATTA TTTTTTTTTT	GATTITATETIA/TRATEGAATCEGATATA/TGTGEGCTEGTTGTTTATAAAATTTTGGTTT 	TANTTAAATAAAAKCTGGAAGCAAAGTATAACCATATGATACTATCATACTACTGGAAACA
2442	22.40	22'90	2450	2410 2572	2470	2640	2540	2650 2812	2710	2770	2830	28890 4052	2750	1010	1070	11.40	1190	09,73
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tetracycline responsive expression vector (TREV), which contains a sequence encoding a fusion protein comprising a transcriptional transactivation domain (TRE) operatively attached to a tetracycline repressor protein (TRE), the first sequence operatively positioned downstream of a promoter. The vector also contains a clouing site operatively positioned downstream of a basal promoter comprising a tetracycline operator. The TREVS can be asset to produce stable cell lines in which gene expression is tightly regulated by tetracycline. They can be used for the production of proteins such as tumon they can be used for the production of proteins such as tumon when the contains which we have contained to the production of proteins such as tumon.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       The present sequence appears in the specification, which describes a
                                                                                                                                                                                                                                                        Minimal promoter, tetracycline responsive expression vector; TREV;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Lightly controlled expression of genes, such as tumour suppressor genes for treating cancers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           New tetracycline responsive expression vectors - used for the
                                                                                                                                                                                                                                                                        transcriptional transactivation domain; TID;
treflacy, Line represso, posterio, TRC Tettacy Line operator;
production; stable cell line; proferin production;
tumour suppressor protein; treatment; cancer; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        by abnormal cellular proliferation, particularly cancers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 3555 BP; 1171 A; 684 C; 654 G; 1047 I; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Disclosure; Pages 145-150; 190pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Zhou Y;
                                                                                                                                                                                                                                                                                                                                                                                                       Loration/Qualifiers
7..2794
                                                                                                                                                                                                                    DNA sequence of the specification.
35.42 TTTAAATGAGGATTATTGATAGT 3554
                                                                                                        AAV54990 standard; DNA; 3555 BP
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                                                                                                                                                                               26-NOV-1998 (lirst entry)
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                                                                                                                                                                                                                                                                                                                                                                     Unidentified.
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                                                                         RESULT 4
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99.78; Score 3383; DR 19; Length 4555;

Hest Local Similarity 100.0%; Pred. No. 0; Matches 3383; Conservative 0; Mismatches

Query Match

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O GATITIACIGCALIAIC 	TI AACT LOGGAGAAGTTTCATCTOTOGATGGGAGTATTGGGAGGTTATATTCAAAGA 	D AAGGAACTGTGGGGAALCTGTATGCTGTAATTGCAGGAG FELFELFELFELFELFELFELFELFELFELFELFE Z AAGGAACTGTGGGGAATCTGTATCTGCAGGAG	AUTITIAUTGAGGTACMGAAAAGATAGAAAAGAGGGGCGTAAAT 	TTGAAGAA TTGAAGAA	*UV GALGIALIGITIGCACTCTTCAGCAAATTGGAAAGGACACTGGACTTATATTTTGACA 	CAACCCAGNAGTTCGATATCTAGNGAAATACTGCATTGGTTGAAAAATTCTTTTTT 	AFCACATITITATTAGCTAAAGGGGAAGTATTACAAATGGAAGATGATCGTGATT 	499 THEAGHAAIGCIAIGIGECTIGACTATTTTALTAACICTCACCTCCCATGTFIGET HILLIHILIHIHIHIHIHIHIHIHIHIHIHIHIHIHIHI	AAAGAACCATATAAAACAGCTGTTATACGCATATA	F10 GGLCAGAACAGGGGCACGGATACCAAAACAACTAGAAATGATACAAGAATTATTGAA 	GTICLCTGTAAAGAACATGAAUGTAAUATAGAUG TILLTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	TITAIGAATICTCTTGGACTGTAACATCTAATGGACTTCTAAGG 	AATCITTCTAAACGATACGAAGAATTTATCTTAAAAATAAAGATG 	HTTTGGATGATGATAAAGTCTTGAGAGTGATTGTATAGACAGTTTT HTTTTTTGATGATAAAAGTCTTGAGAGTGATTGTATAGAGAGTTT	ACACCACGAAAAAATAACCTTGATGAAGGTGAATGTAATTCCTC 	ATTCAGCAAGTGA 	030 OCTIOAGAAAICIGAITIOCIAITITAACAACIGCACAGIGAATC 	- 2
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Ś	TIII.MAIAIATETTIAIFAAGSIGEGCICIIGAAGSIIGIAAIG 1329
qq	FITTICALAIGETETTATTGGGGGGGGGGGGGTGGTAATGTAATG 1491
ΟY	STAGATOTOAGAALOTIGALICIGGAACAGAITIGICILICOOA 1389
qq	STAPATETCAGAATETTEGTEGTAGAATTEGTETTECCA 1551
δλ	TTAATTTAAAAGCCTTTGATTTTTACAAAGTGATGGAAAGTTTT 1449
qu	ITAATTTAAAAGCCTTTGATTTTTACAAAGTGATCGAAGTTTT 1611
δ	ACTICACAAGAGAATGATAAAACATTIAGAACGATGIGAACAT 1509
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3	TGCARCAGATATGTATGTTCTCCTGTAGATCTCCCAAAGAA 1851
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,	APPAATIATSALGIGGALGIAIGGAALAIGIAAGGAAAGIGAAG 1989
	ACCAAATTATGATGTTGGTTGGTTGTTGTTGTTGTTGTTGTTG
δy	2049
Dp	FAAAAFSAFISTAASASSATASAAASATCTIGGTSATGCTGT 2:11
ΟY	2109
Db	GETTITEATCAAAGAAGAAGATAGAIAGAAIAIAIAGAATIC 2271
δŏ	GGCAGAGACHGAAAACAAAIATTITGCAATATGCTTCCACCAGG 2169
QO	rocacasactoaaacaaa.arrittocactarectrohaceaca u 31
ζ	PATANGICACATICCICGAAGCCTTACAGTITCCTAGITCA 2229

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ESTI: Felomerase, ratalytic subunit, reserve transcripture; literspan:
retinoblastoma: p5%; tumour suppressor; inhibitor; arterioscherosis;
proliferation; immortal; tumour therapy; macular degeneration; activator;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Rb/INK4 pathway, especially an Rb/plsiNK4a pathway. The encoprotein MiM2 is a cellular inhibitor of Rb/EzF function and the p5 tumbour suppressor and can also be used in the methods, other molecules which can be used include cdk4 or cdk6 mitants. In particular, a cdk mutant is one which differs from at one or more of residues Kzz, KZ4, H95 and/or P97.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    lines in vitro and for studies on biochemical and physiological aspects of growth and differentiation. Long lived (immortal) cells could also be of use in the production of normal or genetically engineered
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         The invention concerns methods and reagents for extending the life span,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    New method for increasing the proliferative capacity of cell lines comprises administering agents reversibly activating felomerase activity and reversily iganticating ELTINMA and/or (5) pathways useful
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            e.g. the number of mitotic divisions, of a cell. The method relies on activation of a relomerase activity and inhibition of one or horh of a relimphastoma (Eb)/INK4 pathway or a p53 pathway. Phereforeylation of a by cyclin-dependent kinases, cdk4 and cdk6, releases the cells into the division cycle. Binding of INK4 family members, e.g. the tumour suppressor p16 NK4a, inhibits kinase activity and results in growth agreet. By inactivators can selectively and reversibly inactivate an
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Additional constructs include a papilloma virus E7 profesin, or other viral oncoprocein which bypasses Rb and/or p64. Antisense constructs of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            increasing the proliferative capacity of cells. He cells are subsequently of use in pharmaceutical and cosmetic preparations used to
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3310 GATHTTATACTICAGAATGTAAAAGAATTTATTTTCTTCATCAANTTATGTT 3369
                       Claim 5; Page 121-123; 123pp; English.
                                                                                  3370 TTTAAATGAGGAFTATTGALAGI 3392
                                                                                                                            3532 TTTAAATGAGGATTAITGATAGT 3554
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    in treating age related diseases
                                                                                                                                                                                                                                      AAA29391 standard; DNA; 4839 BP
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                                                                                                                                                                                                                                                                                                                                                                       Human retinoblastoma gene.
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0 3.2.4. TELATARCITTIATGAATTETETETETETAAFAFAFTGGAGTTTGGAGAGGTTGAA 1082 1084 AAICITICIAAACGATACGAAGAAATITAICITAAAAATAAAGATCTAGATGCAAGATTA 1142 AAKACTETTATEAACACTATOCAACAATTAATGATGATTTAAATTCAEGAAGTGATG29 369 303 GATITTACTICA FTATGTCAGAAATTAAAGATACCAGAICATGAGAGAGAGCFFGG 362 70 TIAACITGGGAGAAAGTTTCATCTGTGGATGGAGTATTGGGAGGTTATATTCAAAAGAAA 129 4.2.4. AAGGAACTGTGGGGAATCTGTATCTTTATTGCAGCAGAOCCAAAAAAAGTGGGGGC 48.2 ACTITIACTGAGGTACAGAAAAACATAGAAATCAGTGGCCATAAATGGTTAGTA 249 250 AAAGAAATTGATACCAGTACCAAAGTGATAATGCTATGTCAAGACTGTTGAAGAAGTAT 309 370 CAACCCAGCAGIICGAIAICIACIGAAAIAAATICIGCAIIGGIGCIAAAAAGIIICLIGG 429 4 (C. ATCACATITITATIAGCTAAAAGGGAAGTATTACAAATGGAAGATGATGGTGTGGTGTTTCA 489 724 ATCACATITITATIAGTAAAAGAAAAAAGAAATGSAAGATGATGTGGTGATTTCA 782 490 LITICAGI LAATGOTATGOTOCTTGACTATTTTAAACTCTCACCTCCCATGTTGCTC 549 610 GGTCAGAACAGGAGTGCACGGATAGCAAAACAACTAGAAAATGATACAAGAATTATTGAA 669 520 CITCLCLCLGTAAAGAACATGAATGTAATATAGATGAGAGAAAAATGTTTGAAAAAT 729 MSO TITTIGGATGATGATAAAACICTTGAGACTGATTCTATAGACAGTTTTGAAACAGAGA 909 910 ACACCACSAAAAAGTAACCTTGATGAAGGTGAATGTAATTCCTCCACACTCCAGTT 969 FIG. AAGGAACTGTGGGGAATCTGTATGTTTGCAGGAGTTGACCTAGATGAGATGTGGTTC 189 48 1 ACTITIACTGAGGTACAGAAAACATAGAAATCAGTGTCCATAAATTGTTTAACTTACTA 542 550 AAAGAACCATATAAAACAGCTGTTATACCCATTAATGGTTCACCTCGAACACGAGGGGA 609 Gaps 290 AATCTTTCTAAACGATACGAAGAAATTTATCTTAAAAATAAAGATCTAGATGCAAGATTA 310 GAIGTA!!GTTTGCACTCTFCAGCAAATFGGAAAGGACAIGIGAACTIAIALAFFTGACA 303 OGTCAGAACAGGAGGCACGGATAGCAAAACAACTAGAAAATGATACAAGAATTATTGAA ** TITATACCITITATGAATICTCTTGGACTTGTAACATCTAATGGACTTCCAGAGGTTGAA DB 21, Length 4839; Indels Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other; 0; 0; Mismatches 99.7%; Score 3383, 3 Matches 3383; Conservative Local Similarity Onery Match े . Ē ŝ ŝ S Ē > 5 3 ŝ <u>a</u> $\stackrel{>}{\sim}$ # Š ŝ Ę 3 3 3 $\tilde{\Xi}$: *· Ś Ē Š

5971 1629 1090 CTGAAAAGGTGAAGGATAIAGGAIACAICTTIAAAGAAATTIGCIAAAGCIGTGGGA 1149 1150 CAGGGTTGTGGAAATTGGATGGAGGGATACAAACTTGGAGYTGGCTTGTATTACCCA 1209 1443 CAGGGTTGTGTGGAAATTGGATGAAGGATACAAATTGGAGTTGGTTTGTATTACGGA 1592 1503 GTAATIGGAAYCCATGCTTAAATCAGAAGAAGAACGATTATCCATTCAAAAFTTFFAGGAAA 1562 1270 CTTCTGAATGACAATTTTTTATATGTCTTTAILGGGGGGGGGGTCTTGAATG 1329 1330 GCCAÇATATAGCAGAAGTACATÇTÇAGAATÇTTGALTGTGGAAGGAGALTTGTGTTLGCCA 1389 2050 CAGGAGACATTCAAAACGTGTTTTGATCAAAGAAGAGGAGTATGATTGTTATTATAATAATATT 2109 2943 CAGGACATICAAACGTGTTTTGATCAAAGAGAGAGATCTATTATATAAGATTC 2402 1263 AGGACTGTTATGAACACTATGCAACAATTAATGATGATITAAATTGAGGAAGTGATGAA 1322 1630 CICCAGAAIAAICACAGTAGAGAIAIAIAIIIGIGGIGIAAGAICTGCAAAGAA 1689 1750 TTCCAGACCCAGAGCCATTGAAATCTACCTCTCTTTCACTGTTTALAAAAAAGGGTAT 1809 1810 CGGTAGO TATOTO GGOTAAATAO AO TIGIGAA TGO OTTOTGAGGACCCAGAA 1869 1870 TTAGAACATATCATCTGGACCCTTTTCCAGGACCCTGCAGAATGAGTATGAACTGATG 1929 1930 AGAGAGGGATTIGGACCAAATTATGATGTGTTGCATGLATGCCATATGCAAAGTGAAG 1989 2283 AATATAGAGCTTAAATTCAAAATCATTGTAACAGCATACAAGGAICTTCGTCATGCTGTL 2342 1390 INGGAFIP INGAARING TEAATITTAAAAGG TITTINGAAAAGIGAAAGTI EL HELLITELLE H 1210 GTAATGGAATGTATGTTAAATGAGAAGAAGAAGALIAIGCAIICAAAAIIIIAGGAA 1450 ATCAAAGCAGAAGGAAACTTGACAAGAAAATGATAAAACATTTAGAACGATGTGAACAT 1510 CGAATCA1GGAAFCCCTTGCATGCCTCTCACATTCACCTTTATTTGAFCTTATTAAACAA 1803 CGAATCALGGAATCCCTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAAAAAA 1923 CHOCAGAABAAHCACACTGCAGCAGATATGIATGTTTGTGCTGTAAGATGTCCAAAAAAA 1983 AAAGGTICAACTACGCGTGTAAATICTAGTGCAAATGCAGAGACACACAAAGGAACCTCAAAA 2223 AGAGAGGGATTTGGACGAAATTATGATGTGTTGCATGTATGGGATATGGAAACTGAAA 1743 ATGAAAGGAAAGGAAAGTTGAGAAGAAATGATAAAAAGATTTAGAAGGATGTGAAGAT 1570 TCAAAGGAAAGAAGGAAAAAATGAAGTTGAATGTGETTGGAATGTGGTGGTGGTTAATGTTGG 1990 AATATAGACCTTAAATTCAAAATCATTGTAACAGCAIACAAGGATCTTGCTCATGCTGTT ò qq ò qq qq qq qq qq á ò ò δŏ q ò ŷλ

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                                                                2463 COCCUTACCITGTCACCAATACCTCACATTCCTCGAAGCCCTTACAAGTTTCCTAGTTCA 2522
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lacilitate the development of screening assays to evaluate the potential
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     The present sequence encodes a human androque receptor coactivator designated Rb. Androque receptor to activator proteins from the present invention can be used in screening assays to identity candidate
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     of androgen receptor co-activators such as those of the invention will
                  1250 TAATTAAATAAAAGCTGGAAGCAAAGTATAACCATATACTACTACTACTACTGAAACA +409
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Novel androgen receptor-associated proteins used to detect androgenic or antiandrogenic activity in screening assays for candidate pharmaceutical molecules which promote or inhibit the activity \gamma
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    interaction of androgen receptors and androgen responsive elements to modulate androgenic activity. The identification and characterisation
                                                                                                                                                                                                                                                                                                                                                                                                                                             Human, androgen receptor coastivator, ARA54, ARA54, ARA24, detection;
Rb, androgenic, antiandrogenic; identification; prostate cancer; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     pharmaceutical molecules for the ability to promote or inhibit the
                                                                                    1190 GATTITATITIACIAITGGAATCTGATAIACTGTGCTTGTTTTAIAAAAITTTGCTTT
                                                                                                                                3310 GATTTCATACCTCAGAATGTAAAAGAACTTACTGALLATTTTCTTCATCCAACLTATGTT
                                                                                                                                                                                                                                                                                                                                                                                                              Human androgen receptor coacticator Rb eacoding CDMA SBQ ID NOST.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           /note- "androgen receptor coactivator"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      efficacy of drugs in the treatment of prostate cancer.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Claim 8; Page 47-53; 59pp; English.
                                                                                                                                                                                                                 3663 TTTAAATGAGGAFFALIGAFAGT 3685
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14-SEP 1998;
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t Local Similarity 100.08; Pred. No. 0; ches 3383; Conservative 0; Mismatches 0; Indels 0; Caps	10 GATITTACTGCATTATGTCAGAAATTAAAGAATACAGATGATGATGAGAGAGA	70 FTAACTIGGGACAAAGTTTCATCTGTGGGATGCATTGGGAGGGTTATTGCAAAGAAA 128 FTAACTIGGGAGAAAAATTTCATCTGTGGATGAGTTTGTGAGGATATTGTATTGATGAATGTAGAGAGTTATATTGAAAAAA	13.0 AAGGAACTGTGGGGGAATGTGTTATTGCAGCAGTTGACGTAGATGAGATGTGGTTGTTTTTTTT	190 ANTITIACIGAGCIACAGAAAAACAIAGAAAICAGIGICCAIAAAITCIIIAAGIIACAA 240 	250 AAAGAAA IGATACCAACTACCAAAGIIGAWAA WOTTATGICAAGACIGTIGAAGAAGTAT 309 311111111111111111111111111111111111	110 GATGTATTGTTTGCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATATA	420 PANCCASCAGINGAIAICHACHACHAAAIAAATGIGGAINGGIGCIAAAAGINCTIGG 420 	430 AFCACATHTATTACTAAAGGGGAAGTATTACAAATGGAAGTGATCGGTGATTTCA 488 	490 ILICAGI HAATOGTAUGTGTCCTTGACTATTTTATTAACTCTCACCTCCCATGTTGCTC 540 ILILILILILILILILILILILILILILILILILILIL	550 AAAGAAYOZIZIZAAAAAAGGIGITZIZAOCCATTAATGGITCACCICGAACACCCAGGGGA 606 1111.11.1111111111111111111111111111	610 OGITAGAACAGGAGGCACGCATAGCAAACAACTAGAAATGATGACAAGAATTTATGAA 668 + 12141214111111111111111111111111111111	F26 OTFCEGTAAAGAAGAAGAAGAATGTAATATAGATGGGGGAAAAAGTETTATTCAAAAY 728 	730 ITTATACCITITATGAATICTCITGGACITGTAACALCTAATGGACITCCAGAGGTIGAA 780 ITTATATACTATTATGAATTCTCITGGACTITGTATTTTTTTTTT	796 AARCHILCHAAAGGARACGAAGAAATHAFCFFAAAATAAAGAFCFAGATGCAAGAFFA 848 	850 IFFILGRATCATGATAAAACTCTTCAGACTGATTCTATAGACAGTTTTGAAACACAGAGA 909 	910-ACACRASAAAAARTAACCTIGATGAAGAGIGAATGTAATTCCTCCAAAAATCCCGCAGT 966 1219-AACCAASAAAAAGIAACCIISAIGAAGAGGGAAIGTAATTCCTCCACACACCCAGTT 126 1203-AACCAASAAAAAGIAACCIISAIGAAGAGGGAAIGTAATTCCTCCACACACCCGAGTT 126	970 ADGACTGTHATGAACACTATCCAACAATTAATGATTTTAAATTCACCAAGTGATCAA 105 	isto celegaaaareega electafitiaacaachgaacagaga egaagaaagaata 106
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cytostatic; gene therapy; antineoplastic; Wilm's tumour; ademocareinoma;
3310 GATTICATACCICAGAATGTAAAAGAACTTACTGATTATTTTCTTCATCAACTTATGTT 3369
                                             Breast cancer related gene sequence SEQ ID No:1210.
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ensophageal, ovarian, kidney, prestate or panereativ sancer, astenocarcinoma, carcinoma, clear cell cancer, infiltrating ductal cancer, infiltrating lobular cancer, squamous cell carcinoma, neuroconductine
                                                                                                                                                                                                                                                                                                                                                                                                            The present invention describes a method (MI) for screening for an anti-inceptatic agent. The method involves exposing cells to a chemical anti-inceptatic activity, determining a change in expression of at least one gene (1) of a signature gene set, where (1) comprises a sequence (8) selected from 8447 sequences (given in ABLEB1664 to ABL20110), or is at least 95% identical to (8), where a change in expression is indicative of anti-neoplastic activity. (1) has eytostatic activity and can be used in gene therapy. Mican be used for screening as anti-neoplastic agent, and can be used for producing a product which is the data collected with respect to the until neoplastic agent as a structure and the data is sufficient to convey the chemical structure and and the data is sufficient to convey the chemical relational treatment of cancer such as colon, breast, stomach, lung, thyrold,
                                                                                                                                                                               Horrigan S,
                                                                                                                                                                                                                                                                                   Surpening for anti-neoplastic agent involves exposing cells to a chemical agent to be rested for anti-neoplastic activity and determining a change in expression of a gene of a signature gene set
                                                                                                                                                                             Augustus M. Carter KC, Ebner K. Endress G,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Sequence 4839 BP; 1534 A; 902 C; 880 G; 1523 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                arcinoma, papillary carcinoma and Wilm's tumour.
                                                                                                                                                                                                                                                                                                                                                                        ID 1210; 44pp; English.
                    2000US-237606P.
2000US-237608P.
                                                               2000US-244867P.
2000US-245084P.
                                                                                                                                                                                                    Weaver Z;
                                                                                                                                    (AVAL.) AVALON PHARM.
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NOV-2000;
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Locy March 99.7%; Score 3383; DB 24; Longth 4839; Hest Locat Similarity 100.0%; Prod. No. 0; 0; Indels 0; Gaps Matches 4883; Conservative 0; Mismatches 0; Indels 0; Gaps

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130 AAGGAANTGROOGGAARGYGYATGYTTTATHGGAGCAGNTGACCYTAGAYGAGALGYGGING 189 AICACATTITATAACIAAAA3GSCAAGTATACAAATGGAAGATGATCTGGTGATTCA 489 *6 * ITAANTIGGGAAAAAAAATTICATCTGTGGATGGAGTAITGGGAGGATTATATICAAAAGAAA 422 42 f AAGGAANTGTGGGGAATCTGTATCTTTATTGCAGCAGTTGACCTAGATGAGATGTCGTTC 482 AAAGAAAIIGAIACCAGIAACAAAGIIGAAAAGGIACIAAGAAGGIGIAAAG 310 GAEGEALETFEGGACTCTTCGAGAATTGGAAAGGACATGTGAACTTATATATTTGACA 369 PAACHONINGANTECHATATCTACTCAAATAAATTCTGCATGGTGGTAAAAGTTTCTTGG 429 663 CAACCCAGCAGTTCGATATCTAGTGAAATAAATTCTGCATTGGTGGTAAAAGTTTGTTGC 722 ŝ ã 2 ä $\widehat{\varsigma}$ = 3 Š $\stackrel{\searrow}{\sim}$

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723 ATCACATITITATIAGGIAAAGGGGAAGIAIIAGAAAJGGAAGAIGAIGIGGGGAATIICA 782
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                                                   490 PEPICAGTTAATGCTATGTCCTTGACTATTTATTAAACTCTCACCTCCCALGIIGCIC 549
                                                                                                                                                                     550 AAAGAACCATATAAAACACTGTTATAACCCATTAATGGTTCACCTCGAACACCAGGCGA 609
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    the detection and treatment of a defective human gene related to
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              99.7%; Score 3381.4; DB 15; Length 4597;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              blaamosing the presence of defective retinoblastoma alleles comprises comparing genetic material corresponding to a normal comman retinoblastoma with DNA from a patient.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Best focal Similarity 100.0%, Fred. No. 0,
Matches 3382; Conservative 0; Mismatches
                                                                                                                                                                                                          (MASS-) MASSACHUSELIS EYE & EAR INFIRMARY.
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                                                                                                                                                                                                                                              (WHED ) WHITEHEAD INST BIOMEDICAL RES
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                                                                                                                                         86US-0895163.
                                                                 87EP-0307095.
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PSDB; AARS8568.
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1984-1984
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970 AGGACTGTTATGAACACTATGCAACAATTAATGATGATGATTTAAATTGAGGAAGTGAGGAAGTGAA
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                                                           610 GGTCAGAACAGGATGCACGGATAGCAAAACAACTAGAAAATGATACAAGAATTAITGAA 669
                                                                                          670 GTTCTCTGTAAAGAACATGAATGTAATATAGATGGTGAAAAATGTTTATTTCAAAAAT 729
                                                                                                                                                                                                              730 TITATACCITITATGAAIICICIIGGACIIGIAACAICIAAIGGACIICCAGAGGIIGAA 789
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2890 CCAAACTAAAATTGCTGTGTTTAFGGAAGAAGGGGCCTAGAAGGGGGAGTCCTGA 2949
                                                                                                                 31.40 CTCTTCTGCAAAAATGGATATTATTAGAAATTAGAAAATTACTAAATTACTAATTTACAAAATTA 4189
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                                                               2986 AGATTGAAAATCTTGTGTAAATCCTGCCATTTAAAAAGTTGTAGGAGTTGTTGTTGTT 4045
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2770 GAIGGAATICTITGGGISATICCTIAAGGGACTISAAATGITTAGICATGATGATTATTATAGA 2829
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                                                                                                                                                                3310 GATTTCATACCTCAGAATGTAAAAGAACTTACTGATTATTTTCTTCATCCAACTTATGTT
                                                                                                                                                    2950 TAACCCAGGCCIGICIGACIACTIIGCCTICIIIIGIAGCAIAIAGGGGATGTIIGCTC
                                                                                                                                                                                                                                                      3070 GECCEAECEAECTECAAALGCAALEEGALEGACEGALECAALEAAAALIATOTEGAA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Human retinoblastoma gene cDNA.
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11:AUG-1986;
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debe can also be used to synthesize Rb polypeptide (see AAV01542) for used in the treatment of individuals defermined to bove a defective as also as also.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   446 ACTITIACTGAGCTACAGAAAAACAIAGAAAICAGTGICCAIAAAIICITIAACITACIA 405
                                                                                                                                                                                                                                                                        analysing predisposition to retinoblastoms and for the detection and treatment of retinoblastoms
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 0; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          This is the nucleic acid sequence of a cDNA of the normal human retinoblastoma gene Rb. Absence or mutation of the Rb gene (see iso AAXO4502) predisposes an individual to retinoblastoma. To isolate Rb cDNA, the human DNA probe pH3 8, isolated from a human chromosome 13 lambda phage library, was used in a chromosome walk to isolate and map 30 kb of genemic DNA surrounding the H7-R sequence. Fragment p7H90 TYTCC 97500) was obtained, and was sequence. It is a probe to series a cDNA library that had been constructed from an adenovirus 12 transformed human embryonic retinal celling. This provided clone pf 7k (ACC 97343) which in northern those cross-reacted with a 4.7 kb transcript in transformed retinal cells which was not present in 4 telinoblastoma and one
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         250 AAAGAAATTGATACCAGTACCAAAGTTGATAATGCTATGTCAAGAGTGTTGAAGAAGTAT
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          retinal cells which was not present in 4 retinoblastoma and one steosarcuma cell samples. By nucleic acids comprising the Rb nope change of the group such as now of the 25 ex-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               of 26 introns, can be used in a claimed method for detecting a deletion or point mutation in the Rb gene of a human patient.
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88US-0146525.
89US-0300667.
                                              920S-0951342.
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                                                                                                                                                                                                                     WPI; 1999-094898708
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                                                                                                                                                                                                                                            P PSDB; AAY01542.
  21-JAN-1988;
23-JAN-1989;
                                                                     (S. Q.1 - 1992)
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Modified retinoblastoma tumout suppressor, KISP protein; rancer therapy; cellular proliferation inhibitor; ss.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                        proliferation, particularly cancers. The PTSPs have a broader spectrum of activity than wild type RTSPs.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Sequence 3554 BP: 1170 A; 683 C; 653 G; 1048 T; 0 other;
                                                                                                                                                                                                                                                                                                                        inhibiting cellular proliferation, particularly cancer
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0: Mismatches
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                                                                                                                                                                                                        Hu S, Xu H, Zhou Y;
                                                                                                                                               (BAYU ) BAYLOR COLLEGE MEDICINE. (TEXA ) UNIV TEXAS SYSTEM.
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712 AAAGAACCATATAAAACAGCTGTTATACCATTAATGGTTCACCTCGAACACCCGGGGG 77]
                                                                  610 GGTCAGAACAGGAGIGCACGGAIAGCAAAACAACIAGAAAAIGAIACAAGAATTAITGAA 669
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2932 GATGGAATTGTTTGTGTTGCTAAGGCACTGAAATGTTAGTCATTGTATTAATAA 2991
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2770 GATGCAAFTGTTTGGGLGATTCCFAAGCCACTTGAAATGTTAGTCATTTTATTATATACA 2829
                                                                                                                8052 CCAAAGTAAAATTGCIGTGCITTATGGATAGTAAGAAIGGCCCITAGAGTGGGAGTCCTGA 3111
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                                                                                                                                                                                                   Magnosis of retinoblastoma · using genetic material corresp, to a normal
                                                                                                                                                                                                                                                                                                                                                                                                       toaplasm. It is used to produce an antibody to the protein, contacting this with the tumour sample and detecting immune complexes as indication of the presence is the tumour sample of the protein. Whole sequence or a unique sub-region can be used. The method identifies patients lacking the defective retinoblastoms (Rb) allele and thus are not at risk of
                                                                                                                                                                                                                                                                                                                                                                          1008 gone cannodes a protein, the absence of which is associated with a
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                                                                                                                                                                                                                                       human retinoblastoma gene or a unique sub-region
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                                                                                          1988-065827/10.
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OBBITAR OF TATE OF COMMENTAL OF THE OFFICE OF THE OFFICE OF THE OFFICE OF THE OFFICE O	TIANAACATA KCATCHOGARCCTITICCAGCACCCTGGARAATGACTA KGACCATCATG) AGAGACAGGCATTTGGACCAAATTATGATGTGTTCCATGTATGGCATATGCAAAGTGAAG 	AATALAGACTTAAAFICAAAATCATIGTAACAGCATATAGGATGTTCCTCATGCTGT 	FORGAGACALICAAACGGTTTCAACAAACAAGAGGGGTALGATGATGATAAGAGTATTC TTTTTTTTTTTTTTTTTTTT	TATAACTCGGTCTTCATGCAGACTGAAACAAATATTTTGCAGTATGCTTCCACGGG	COCCTENCITES FOR CANCOALACTE COTTCO COA AGENCE THE CONTROL OF TH) POCTTAPORA IL PERGRADARA ICTATA FILGAPOCTGAAGARICCA FRAAART 	FCAGAAGGEGGGAACACCAACAAAAAAGGCGGAAGAFCAAGAAGCAAGAATCTTAGTATAGAATT HILLIHIHIHIHIHIHIHIHIHIHIHIHIHIHIHIHIHI) GGTGAATCATTCGGGACTTCTGAGAAGTTCCAGAAAATAAAT) dan ottotottaaaaaaattottoaagaabeaneaneeteetaaaeetaaaaaeta) CONTITUATATICAAOGATCAGATCAAGGAAGTAGGAAGTAAACTICECCCAGGAGAGGECC 	AAATITCAGCAGAAACTGGCAGAAATGACTTCTACTCGAACAGGATGCAAAAGCAGAAA) ATGAA IGA LAGGATACC ICAAACAAGAAGAAATGAATGACGATGTCAGGACCTTGGT) GRAPATGIGIATACOPTTROATECATICICICACAGAGGGACTGTATACTTTCCC 	AUGITIC TATTA PARK OF ACAITIAA TATOTIC AGENCITETEGO SAGATATAAAA TATGA CAATA TATAA TATAA AAATA TATAATA TATAATA TATAATA	GARGCAAFIGEFEGGEGAFFCELAAGCAACFIGAAATGETAGEGAFIGETATTATAGA [) AGATTGAAAATCTTGTGTAAATCTTGCATITAAAAAGTGTGTAGCAGATGTTCCTCTT 	CCAAAGTAAAATTGCTGTGCTTTATGGATAGTAAGAATGGCCCCTAGAGTGGGAGTCCTGA
1966	1870	1940	1990	2050	2110	2170	22.80	2290	2450	2410	2470 2626	75.80	2590	2650	2710	2770 2926	2840	0687
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                                                                                                                               3070 GECCEAECTECTECAAA1GCAAFTTGALIGACTGCCCATTGACTAAAATTATCTEGAA 3129
                                                                                                                                              3130 CTCTTCTGCAAAAAGGALATTATLAGAAAITAGAAAAAATTACTAALLITAGAGATLA 3189
                                                                                                                                                                                                                                        3250 TAATTAAATAAAAGGGGAAAGGAAAGTATAACCATALGALACTALCALACTACTACTACTACAAACA 3309
                                                                                                                                                                                                                                                                                                                      3406 TAATTAAATAAAAGCTGGAAGCAAAGTATAACGATATGATACTATGATACTACTGAAACA 4465
                                                                                                                                                                                                                                                                                                                                              3046 CCAAAGIAAAAIIGCIGIGGIIITAIGGAIAGIAAGAAIGGA CIAAGIGGGAAGIGGGAGI CIGA 3105
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Human; retinoblastoma protein; Rb; cytostatic; cancer; apoptosis;
mycolactomic, antisense; breast cancer; bladder cancer; skin cancer;
stomach cancer, liver concer, colon cancer, oral cavity cancer;
lymphoma; leukaemia; qene; ss.
                                                                            Anticancer agent useful for treatment of cancer e.g. of skin.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Human retinoblastoma protein cDNA sequence.
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                                                                                                                                                                                                                                                                                                                                                                                                   3370 TTTAAATGAGGATTATTGATAGT 4392
                                                                                                                                                                                                                                                                                                                                                                                                                  3526 ITTAAATGAGGAITATTGALAGI 3548
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              ABK86079 standard; cDNA; 4740 BP.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 comprising mycolactone
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ABK86079
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The invention relates to an anticancer agent comprising mycolactone.

Also included for is an anticancer agent comprising mycolactone and antiscuss inhibitors of retinoblastoma (RB) protein expression. The anticancer agent is used for the treatment of cancers such as breast, bludder, spin, stomach, liver, colon and oral cavity, lymphoma and bludder, spin, stomach, liver, colon and oral cavity, lymphoma and capta and the Rb inhibitor increases the apoptosis-inducing activity of mycolactone even in Rb positive cancer cells. The agent is specific to connects in which Rb proteins are optionally expressed and mycolactone shows very strong anticancer election vite as in two.

The present sequence is the human cDNA for refinoblastoma protein.

46.4 AGTICTGTGTAAAGAACATGAATGTAATATAGATGAGGTGAAAAATGTTTATTTGAAAA 1022 1923 TITTIATACCTTITATGAATTCTCTTGGACTTGTAAGATCTGAATGGACTTGGAGGTTGA 1982 190 ACTIFIACTGAGCTACAGAAAACATA-GAAATCAGTGTCCATAAATTGTTTAACTTACT 248 249 AAAAGAAATTGATACCAGTACCAAAGTTGATAATGCTATGTCAAGACTGTTGAAGAGTA 308 543 AAAAGAAATTGATACCAGTACCAAAAGTTGATAATGTCAAGACTGTTGAAGAAGTA 602 488 789 AAATCITICTAAACGATACGAAGAAATITATCITAAAAATAAAGAICIAGAIGCAAGAIT 848 3.90 AAGGAACTGTGGGGAATCTGTATCTTTATTGCAGCAGTTGACCTAGATGAGATGTGGTTC 189 469 ACAACCAGCAGTTCGATATCTACTGAAATAAATTGTGCATTGGTGCTAAAAGTTTCTTG 428 63 ACARCCACTIONALATOTACIONAATAAATTOTGCATTGCTGCTAAAACTTTCTTG 722 2.3 GATCACATITITATTAGCTAAAGGGGAAGTATTACAAATGGAAGATGATCTGGTGATTTC 782 169 ATTLICACTIAATGCTATGTGTCCTTGACTATTTATTAAACTCTCACCTCCCATGTTGCT 548 649 CAAADAACCATATAAAAACAGCIGETATAAGGGATTAATGGETTCAGCTCGAACAGGGGG 608 509 AGGTCAGAAACAGGAGTGCACGGATAGCAAAACAACTAGAAAATGATACAAGAATTATTGA 668 * * AGGICAGAAGAGGAGGCATAGGAAAACAAGTAGAAAATGATAGAATTATTGA 962 669 AGLININGTAAAGAACATGAALGTAATATAGATGAGAGAAAATGTTTATTTCAAAAA 728 29 1111414787CTTF14FGAATTC1C11GGACTTGTAACATCTAAFGGACTTCCAGAGGTFGA 788 2, Caps 3.19. IGAIGIALIGITTIGCACTCTTCAGCAAATTGGAAAGGACATGTGAACTTATATTTGAC 184 AC-111ACTGAGCTACAGAAAACATACGAAATCAGTGTCCATAAATTCTTTAGT 429 GATCACATTITIATIAGCIAAAGGGGAAGTATTACAAATGGAAGATGTCTGGTGATTTC 98.7%; Score 3348.8; DB 24; Length 4740; 7; Indels Sequence 4740 BP: 1508 A: 887 C: 862 G: 1483 T: 0 other; O: Mismatches Pred. No. 0; 99.7* Conservative Local Similarity Mathues 3475; Ġ Ē ŝ 압 ें ŝ <u>a</u> S Š <u>.</u> 5 3 ŝ 5

IAGGACIGIIAIGAACACIAICCAACAATIAAIGAIGAITTTAAATICAGCAAGIGATCA 1028 1263 IAGGACTGTIAIGAACACIAICCAACAAITAAIGAIGAITTTAAATICTGCAAGIGAICA 1322 1209 AGTAATGGAATCCATGCTTAAATCAGAAGAAGGATTATCCATTCAAAATTTTAGGAA 1258 1503 AGTAATGGAATCCATGCTTAAATCAGAAGAACGATTATCCATTCAAAATTTTAGCAA 1552 1329 GGTTATATATATATATATATATTTTCAGAAITTIGAIICIGGAACAGAIIIGICIIICCC 1388 1683 ATGGATICIGAATGTGCITAATTITAAAAGCCITTGATTITTACAAAGTGATGGATGTTT 1742 1449 TATCAAAGCAGAAGGCAACTTGACAAGAGAAATGATAAAACATTTAGAACGATGTGAACA 1508 1743 TATCAAAGCAGAAGCAACTTGACAAGAGAAATGATAAAACATTTAGAAGGATGTGAAGA 1832 1569 TOGAALTAIGGAALTTGCAIGCICICAGAIICACCITIATIIGAICITATIAAACA 1558 1629 TCTCCAGANTAATCACACIGCAGCAGATATGTATCTTTCTCCTGTAAGATCTCCAAAAGA 1688 1569 ATCAAAGGACGAGAAGGAAGTGATGAGTTGAATCTGCTTGTCCTCCTTATCTTATCTTGT 1428 1923 TCTCCAGAATAATCACACTGCAGCAGATATGTATCTTTCTCCTGTAAGALGTCCAAAAAA 1982 1689 AAAAGGIICAACIACGCGIGTAAATICIACIGCAAATGCAGAGACACAAGCAACCICAG: 1748 1749 CTTCCAGACCCAGAAGCCATTGAAATCTACCTCTTTCACTGTTTTATAAAAAAGTGTA 1808 2043 CTTCCAGACCAGAAGCCATTGAAATCTACCTCTTTTCACTGTTTTATAAAAAGTGTA 2102 1809 TOGGOTAGOCTATOTOCGGCTAAATACACTIIGIGAACGCCTTOTGTGTGTGACCACCCAAA 1868 909 AACANGAGAAAAASTAACCIIGAIGAAGAGGIGAAIGIAAIICCICCACACACAGI 1089 ACTGAAAAGAGTGAAGGATATAGGATACATCTTTAAAGAGAAATTTGCTAAAACTGTGGA 1149 ACAGGGTGGGGGAAATIGGATCACAGGGAIACAAACTIGGAGTICGCTFGTATIACK 1443 ACAGGTTGTGTGTGAAATTGGATCACAGGGATACAAACTTGGAGTTCGCTTGTATTACCA 1389 AUGGATTGTGAAIGIGGTTTAAAAGGGTTTGATTTTTAGAAAGTGATGAAAAL 203 AACACCAGAAAAAAAACCTTCALGAAGAGGTGAATATAATTCCTCCACACACCCAC 1029 ACCIPICAGAAAAFICFGAFFFFCCFAFFFFFAACAACFFGCAGAGFFGAATCGAAAAGAAGTAT 1323 ACCITCAGAAAAICTGAITICCIAIIITAACAACTGCACAGTGAATGCAAAAAAAAA 1863 ATCAAAGGACCAGAAGGACCAACTGATCACTTGAATCTGCTTGTCTTTAATCTTCC ΟŊ qq a ά QO δ g á qu <u>ئ</u> a qq qq G Ω Ś ò ŏ qq

1929 GAGAGACAPAGGCAPTTPGACCAAATTATGATGTGTTCCATGTATGCCATATGCAAAGTGAA 1988

10 10 10 10 10 10 10 10	DD 3663 TTTTAAATGACGATTAILITITITITITITITITITITITITITITITITIT		XX XX PFEB-1998; 98WO-US03041. XX PF 19-FEB-1998; 98WO-US03041. XX YX PR 20-FEB-1997; 97US-0048118. XX PA (BAYU) BAYLOR COLLECE MEDICINE PA (LEXA) UNIV TEXAS SYSTEM. XX XX XX XX XX XX XX XX XX XX XX XX XX	MP1: 1998-48078871. XX XX PT FINIBILING CELLULAR PROLIFERATION FT INHIBITING CELLULAR PROLIFERATION XX CLAIM 22; Page 158 162; 249pp; 18 XX CC This sequence encodes a modification CC PROTEIN (RTSP) of the invention CC Can be used for treating disease CC PROLIFERATION, particularly can CC CC CC CC CC CC CC CC CC CC CC CC CC
2282 2048 2342 2108 2402 2168 2462 2228 2228 2522 2582	2348 2642 2408 2702 2468 2762	2528 2822 2588 2882 2648	2708 4002 2768, 3062 2828 3122	2888 3182 2948 3242 3008 3302 3068
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otein (RTSP) of the invention. The proteins can be used for inhibiting
thuar proliferation, when coadministered with a p54 protein. The RTSPs
in be used for treating diseases characterised by abnormal cellular
officeration, particularly cancers, the RTSPs have a broader spectrum of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                diffed retinoblastoma tumour suppressor; RTSP protein; cancer therapy;
                                                                                                                                                                                OF TEGETETETATEATERALAGEALATERETABATERAACAGAACACACTEAGAAAALG 3362
                                                        69 TGTCCTATCTATCTACCAAATGCAATTTGATTGACTGCCCATTCACCAAATTATCTGA 3128
                                                                                                                    63 IGTCCTATCTATCTTCCAANIGCAATTTGATTGACTGCCCATTCACCAAAATTATCCTGA 4422
                                                                                                                                                                                                                                                                                                                                                    19 TIAATTAAATAAAAAGCTGGAAGGAAAGTATAACCATATGATACTACTACTGAAAAC + +08
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    03 AGATTICATACCICAGAATGTAAAAGAACTIACIGATIATITICITCATACAACTAATGT 4662
                                                                                                                                                                                                                                                                                                               39 AGATTITATITIACTALIGGAATCIGATATACTGIGCITGITITATAAAATTITGCTT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          4.4 TIAATIAAATAAAAGCTGGAAGCAAAGTAIAAACCATAIGAIACIATCAIACIACTACTACTAC
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hibiting cellular proliteration, particularly cancer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 dified retinoblastoma tumour suppressor gene.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         aim 22; Page 158 162; 249pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        llular proliteration inhibitor; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         nedict WF, Hu S, Xu H, Zhou Y;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 59 TITTAAATGAGGATTATTGATAGT 3392
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                63 PTTTAAATGAGGAPTATIGALAGT 3686
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          758443 standard; DNA; 333 BP.
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Sequence 3323 BP; 1114 A; 605 C; 591 G; 1013 T; 0 other;
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1518 GGAAFGCCFFGCATGCCFCFCAGAFFCACCTFTAFFFGAFCFTATTAACAALCAAGGA 1577 2049 COTOTION THE FILL HITTELL 969 AAATCTGATTTCCTATTTLAACAACTGCACAGTGAALSCAAAAGAAAGTATAGTGAAAAG 1028 1098 AGTGAAGGATATAGGATACATCITIAAAGAGAAAIITGCIAAAAGCIGTGGGACAGGGTTG 1157 1158 TGTGGAAATIGGAICACAGGGATAGAAAGTTSGASTTGGGTTGTAIIAGGGAGIAAIGGA 1217 1149 ATCCATCCTTAAATCAGAAGAAGAACGATTATCCATTCAAAATTTTAGCAAACTTCTGAA 1208 1209 TGACAACATTTTCATATGTCTTTATTGGCGTGCTGTTGAGGTTGTAATGGCCACATA 1268 1269 TAGGAGAAGTACAFCTGAGAATGTTGATTGTGGAAGAGATTIGTGTFFGGGATGGATTGT 1328 1398 GAATGTGCTTAATTTAAAAGCCTTTGATTTTTAGAAAGTGATCGAAAGTTTTATCAAAGC 1457 1458 AGAAGGCAACTTGACAAGAAAATGATAAAACATTTAGAACGATGTGAACATCGAATCAT 1517 1818 CTATCTCCGGCTAAATACACTTTGTGAACGCCTTCTGTGTGGGGCACCCAGAATTAGAAGA 1877 2058 ATTCAAAÇÇIÇITITIĞATÇAAAGAAGAGGAĞTATSALTÇTAHTATAĞIPATTZTALAACTC 2117 1989 ATTCAAACGUSTITETGALCAAGGAGGAGTATGALFCTAFTALAGTGTATAGTC 2048 2118 GBF71 FGA FGAGGAFTGAAAAFAAAIIIIGGAGIAIGGIIIGGAGGGCGCGCIAF 2177 1029 AGTGAAGGATATAGGATACATCTTTAAAGAGAAATTTGGTAAAAGCTGTGGGACAGGGTG 1088 1218 ATCCATGCTIAAATCAGAAGAAGGATTATCCATTCAAATTTTAGCAAAACTTGTGAA 1277 1338 TAGCAGAAGTAPATOTPAGAATGTEGA EFOTGGAAGAGATTEGFOTTFOCOATGGATTGT 1397 1389 AGAAGGTAACTTGACAAGAAATGAIAAAACA11TAGAACGATGTGAACATGGAATGAT 1448 1449 GGAATCCCTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAAACAATCAAAGGA 1508 1698 AACTACGCCFCTAAATTCFACTGCAAATGCAGAGGAGGAAGCAAGCTCAGGCTTTCAGAC 1757 1809 IAICATUIGGACULIIIICCAGUACACUIGCAGAAIGAGIATGAACICATGAGAGACA 1868 1938 GCATTTGGACCAATTATGATGTGTTGCATGTATGGCATATGCAAAGTGAAGATATAGA 1997 1998 CCTTAAATTCAAAATCALTGTAACAGCATACAAGGATCTTCCTCATGCTCTTCAAGAGAC 2057 1329 GAATGEGTTAATTTAAAAGCCTTTGATTTTAGAAAGTGATGAAGGTTTTAAAAGG 1929 CCTTAAATTCAAAATCATTGTAACAGCATACAAGGATGTIGGTGATGTIGGTGTITGAGGAGA q ò 셤 Ο̈́ Ġ ð d ô Ś 셤 qq 셤 qq qq 40 ò qq ò ã Οy ò g ò 9 0ò ô ò

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3318 ACCYCAGAAYGYAAAAGAACTIACYGAYTATTITCYTCATCCAACYTATGTTTTTAAATG 4377
                                                                       3189 TAAAAGCTGGAAGCAAAAGIATAACCATATGATACTATATAACTACTAGTGAAAGATTIGAL 4248
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     osteobarcoma, fibrosarcoma, soft tissue sarcoma, small cell sarcoma, esp. of the lung, melanoma and mammary tumonts.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           190 ACTITIACIGAGCIACAGAAAAAGATAGAAATCACACATAAATTCTITAACTTACTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              97,48; Score 4305,4; DB 9; Length 4579;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Detecting pre-disposition to develop - using retinoblastomma gene probes to detect defects in the retinoblastomma.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          The probe can be used to detect tumour with an Rb detect eq
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           mdels
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                                                                                                                                                                                                                                                                                                                                   Probe; retinoblastoma; tumour; ss
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                                                                                                                                                                                                                  AAN81261 standard; cDNA; 4579 BP.
                                                                                                                                                                                                                                                                                                       Probe for retinoblastoma gene.
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Matches 3354; Conservative
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iş ş	~ ~	ATAAAACASCTGTTATACCCATTAATGGTTCACCTCGAACACCCAGGGGA TITTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	609 751
<u>ئ</u> چ	610	ACCGATACCAAACAACTAGAAATGATACAAGAATTATTGAA FELLIHIHHHHHHHHHHHHHHH CACGATACCAAAACAACTAGAAATGATAC-AGAATTATTGAA	
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¥ 3	3.5	HITATACHTTIATGARTCPOTTGGACTTGTAACAPCTAATGGACTFCCGGGGGTTGAA HITHTHTHTHTHTHTHTHTHTHTHTHTHTHTHTHTHTHT	789
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1650 CGAATCATGAATCCTTGCATGGCTCTCAGATCACCTTATTTGATCTTATTAACAA 1769
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Modified retinoblastoma formour suppressor gene.
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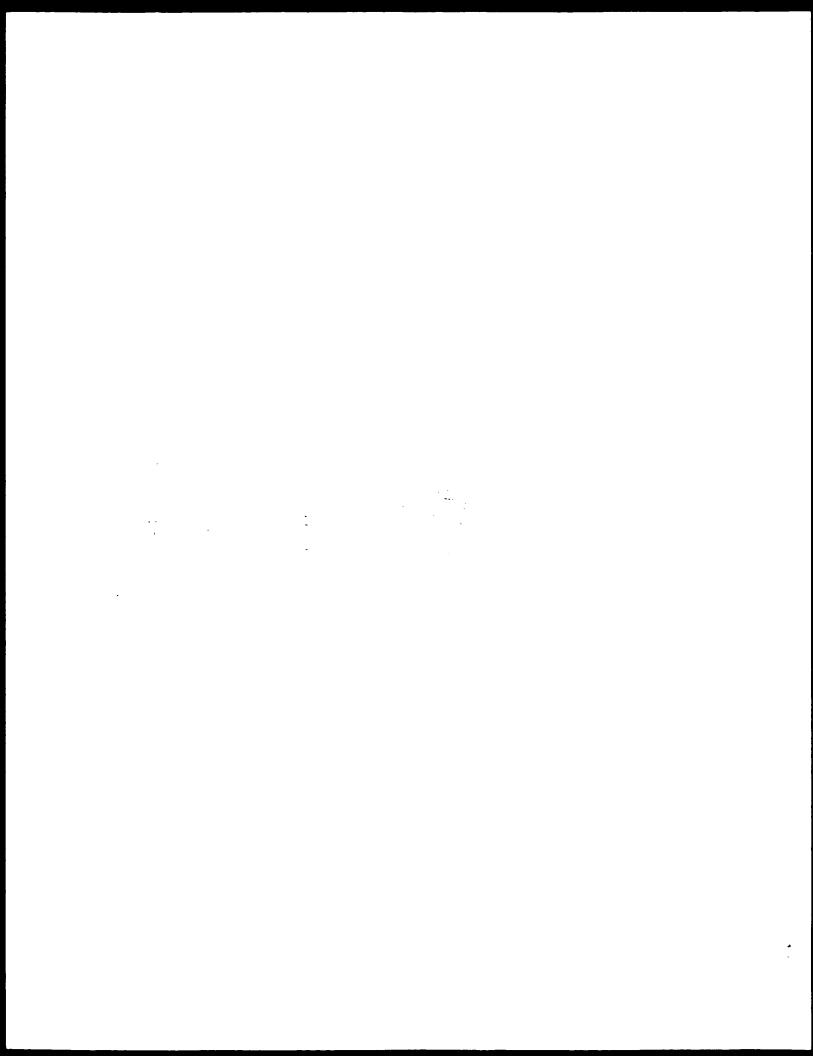
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protein (RTSP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p54 protein. The RTSPs can be used for treating diseases characterised by abnormal cellular proliferation, particularly cancers. The RTSPs have a broader spectrum of
           Modified retinoblastoma tumour suppressor; RTSP profein; cancer therapy;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              476 AGGAGTTGGATATGTACTGAAATAAATTCTGCA11GG1GG1AAAAAG111C11GGATCACA 43S
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              This sequence encodes a modified retinoblastoma tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                         Retinublastoma supplessor protein with N-terminal modification inhibiting cellular proliferation, particularly can of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     96.0%; Score 3257; DB 19; Length 3266;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Sequence 3266 BP; 1092 A; 602 C; 574 G; 998 T; 0 other;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Pred. No. 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                     Claim 22; Page 166-170; 249pp; English.
                            cellular proliferation inhibitor; ss.
                                                                                       Location/Qualitiers
7..2505
                                                                                                                                                                                                                                                                                                                 Hu S, Xu B, Zhou Y;
                                                                                                                                                                                                                                                                     (BAYU ) BAYLOR COLLEGE MEDICINE
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=
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                                                         Homo sapiens
                                                                                                                                                                                                          19-FEH-1998;
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                                                                                                                                                                              27 - AUG - 1998.
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SHMMARIES

		Description	Modified retinobla	Modified retinobla	DNA sequence of th	Human retinoblasto	Human androgen rec	Breast cancer rela	Modified retinobla	Human retinoblasto	Muman retinoblasto
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ALTGNMENTS

AAVS8441 standard; DNA; 3455 BP. AAV58441; RESULT 1 AAV58441

02-DEC-1998 (first entry)

Medified refinchestanta tamost suppressor gene.

Modified retinoblastoma tumour suppressor, KTSP protein, cancer therapy; cellular proliferation inhibitor; ss.

Homo sapiens.

Location/Qualifiers 7..2694 /*tag= a Key

W09837091-A2.

27-AUG-1998.

98WO-US03041 19-FEH-1998;

97US-0048118. 20-FEB-1997;

(BAYU) BAYLOR COLLEGE MEDICINE.

(1EXA) UNIV TEXAS SYSTEM.

Benedict WF, Hu S, Xu H, Zhou Y;

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                                                                                                                                                                                                             protein (RISP) of the invention. The proteins can be used for inhibiting certicular proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnormal cellular
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                                                                     Refirablastoma suppressor protein with N-terminal modification
inhibiting cellular proliferation, particularly cancer
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WFI; 1998-480788/41.
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841 CCAGAGGTTGAAAATGTTTGTAAAGGATACGAAGAAATTTTATGTTAAAAATAAAGATGTA 930
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<i>^</i>	8.5	TATGAACTCAIGAGAGACAGCATTGGACCAAATTATGATGTGTTCCATGTATGGCATA	2040
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5 4	2161	ATTATA FRATTOTATAACTOS STOTTOATS SOGAGACTGAAAAACAAATATTTTGCAGTAT 	2220
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5 3	2281 2281	TTPCTAGETCACCCTACGGATTCCTGGAGGGACATCTATATTTCACCCTGAAGACT 	2340
S =	2 14 1	CCATATANAATTTCAGAAGGTCTGCCAACAACAAAAATGACTCCAAGAGGTCAAGAATC 	2400
Á á	2401	TTAGTAPCAATTGGTGAATCATTGGGGACTTCTGAGAAGTTCCAGAAAATAAAT	2460 2460
451	2461	GLATCHANTAGGGGGGGGGGGGGAAAGAAGGAGGGGGGAGGGAAYYYGTGGGAAAGCA HTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	2520 2520
5 3	2521	CTGAAAAAACTAGGATTTGATATTGAGGATCAGATGAAGGAGGAGTGGAAGTAAACATCTC 	2580 2580
S 4	2581	CTARGAGAGECTAAATTETAGAAACTGGGAGAAATGAFECIACTCGAACACGAATG - - - - - - - - - - - - - - - - - -	2640
6 q	2641	PAAAAGTAGAAATGAATGATAGCATGGATACCTCAAACAAGGAAGAGAAATGAGGATCT 	2700 2700
5 3	2701	CARRANCTTOGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG	2760 2760
<u> 5 </u>	2761	TATAACTTTCCCASSTTCTGTTTATGSCCACATTTAATATCTCAGGTCTTTTTGTGGGTT	2820 2820
40	2821	ATAAAATGEGAATGETAATTGETAGGGAACTEGTAAGGCACTTGAAATGTTAGEGATTTTTTTTTT	2880 2880
5 3 5	2881	GITATTATACAAGATGAAAATCITGIGAAATCCIGCCATTAAAAAGITGIAGAAAGITGIAH HAAAAAGITGIAAAAAGITGIAAAAAGIGIGAAAAGIGGAAAAAAAA	2940
25	2941	TESTITECT CITECAAAGITAAATIGCTGI GCTITAI GGATAGAAATGGCCGTAGAG	3000

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Modified retinoblastoma tumour suppressor; KISP profesu; cancer therapy; cellular proliferation inhibitor; ss.
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2941 TIGITICCICITCCAAAGTAAAATIGCTGIGCHIAIGGAIAGIAAGAAGGGCCTAGAG 3020
                                                              3001 TGGGAGTGGTGATAACCCAGGGTF74CTGACTATHTGCGTTCTHTHGTAATATAGGT 4060
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(TEXA ) UNIV TEXAS SYSTEM.
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                                                                             protein (RISP) of the invention. The proteins can be used for inhibiting cellular proliferation, when coadministered with a p53 protein. The RISPs can be used for treating diseases characterised by abnound cellular
                                                                                                                                                           proliferation, particularly cancers. The RISPs have a broader spectrum of activity than wild type RISPs.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    63 ACTIOALLITACIONATTALCICAGAATTAAAGATACCAGAGGATGTGAGAGAGAGAGG 128
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                                                       This sequence encodes a modified retinoblastoma fumour suppressor
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Pred. No. 0;
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Pischosure, Puge 121 126, 247pp; Unglish.
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                                                                                           1008 ATTATTTTGGATCATGATAAAACTCIICAGACIGALICIAIAGACAGITTTGAAACACA 1087
                                                                                                                                            969 CACAACACCACAAAAAGTAACCTTGAFGAAGGGFGAATGTAAFFFCCTCCACACACACTOC 1028
                                                                                                                                                                                                                                           1029 AGTIAGGACIGIIAIGAACACIAICCAACAATIAAIGAITTIAAATICAGCAAGIGA 1088
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                                           909 ATTATTTTGGAICATGATAAAACTGTTCAGACTGATTGTAGACAGTTTTGAAACACA 968
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Minimal promoter, tetracycline responsive expression vector, TREV;
transcriptional transactivation domain; [110]
3069 CTCTTGTTTTTATTAATTTATATGTATATTTTTTTTAATTTAACATGAACACOOTTAGAAA
                                                                                                                                                        249 ATTAGATITIATITIACIAITGGAATCTGAIATACIGIGIGGGTITITIATAAATTTTC
                                                                                                                                                                                3348 ATTAGALTITATTITACIALIGGAATCIGALATACIGIGGIIGITITATAAAAIIIIG
                                                                                                                                                                                                                                  3869 AACAGATITCATACCICAGAATGTAAAAGAACITACIGATTATTI FCLICALPYAACTIA
                                                                                                     3189 TGAACTCTTCTGCAAAALGGATATTATTAGAAATTAGAAAAAAATTACTAATTTLACA
                                                                                                                    3129 ATCHGFCCTATCTATCTTCCAAATGCAATTTGATTGACTGCCCATTCACCAAAATTATCC
                                                               New Tetracycline responsive expression vectors—used for the 
Lightly controlled expression of genes, such as tumour suppressor
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              used for the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            tetracycline repressor protein; TRF; tetracycline operator; production; stable cell line; protein production; tumour suppressor protein; treatment; cancer; ss.
                                                                                                                                                                        New tetracycline responsive expression vectors
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Disclosure; Pages 145-150; 190pp; English.
                                                                                                                                                                                                                                                                                                                 3429 TGTTTTAAATGAGGATTAITGATAGT 3455
                                                                                                                                                                                                                                                                                                                               3528 TGTTTTTAAATGAGGATTATTGATAG1 3554
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7..2793
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           DNA sequence of the specification.
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The present sequence appears in the specification, which describes a

they can be used for the production of proteins such as tumour suppressor proteins which can be used for treating diseases characterised 7.9 ACCIGATITIACIONAFTATGINADAAATTAAAGATAGCAGATGATGATGAGAGAGAGAG 128 | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | HILL | 129 GACANAACCCAGCAGTTCCATALCTACTGAAATAAATTCTGCATTGGTGCTAAAAGTTTC 488 189 TIGGALFAGAFIITIAITAGIAAAGGGGAAGTATTACAAATGGAAGATGAIGTGGTGAT 548 SCICAAAGAACCATATAAAAACACTGTTAFAQCCATTAATGGTTTCACTCGAACACCCAG 668 289 AAATTITTATGAATTCTCTTGGACTTGTAACATCTAATGGACTTCCAGAGGT 848 129 IIGGITAANTIGGGAGAAAGTIIGAICTGTGGAGAGTATTGGGAGGTTATTGTAAA 188 189 GAAAAAAGGAAFGTGFFFATGTGTATTTAFFGCAGCAGTTGACCTAGAFGAGTGTC 248 249 GIIMACIIIFACIMAGMAAAAAAAAAAAAGAAATGAGMAGATAAAITGMTAACTT 308 409 ACTAAAAGAAATTGATACCAGTACCAAAGTTGATAATGCTATGTGAAGAGTGTGTGAAGAA 368 469 GTATGATGTATTGTTTGCACTCTTCAGGAAATTGGAAAGGACATGTGAACTTATATATTT 428 HB ITGGALPAGALTITIALIAGGTAAAGGGGAAGTATTACAAATGGAAGATGATCTGGTGAT 647 549 TICATIFCAGITAATGCTATGTGTCCTTGACTATTTATATAAACTGTCACCTCCCATGTT 608 Caps tetracycline responsive expression vector (IREV), which contains a sequence encoding a lusion protein comprising a transcriptional transactivation domain (TTD) operatively attached to a tetracycline repressor protein (TTB), the first sequence operatively positioned downstream of a promoter. The vector also contains a cloning site downstream of a promoter. The respectively positioned downstream of a basal promoter comprising a letracycline operator. The TREVs can be used to produce stable cell lines in which gene expression is tightly regulated by tetracycline. 5.28 GACACAGCAGCAGTTCGATATCTACTGAAATAAATTCTGCATTGGTAAAAACTTTC 228 TIGGITAAÇTIGGAAAAATTICATÇIGTGGATGGAGTATTGGGAGGTTATATTCAAAA 448 GITCACITTIACTGACCTACAGAAAAACATAGAAATGAGTGCCATAAATTCTTTAACTT 4...8 ACTAAAAGAAATTGATACCAGTACCAAAGTTGATAAFGCTATGTCAAGACTGTTGAAGAA 18 LICALLICACTIANICCIALGICITGACIALITITATTAAACTCTCCCCATGTT TERT GOGGOOD PROAPPROAPPROGRANG CAALAGCAAAGETAGAAAT GATAGAAGAATTAT ** B. OCCAGGLGACACCACGGACTCCACTACCAAACCAACTAGAAAATGATACAAGAATTAT 229 IGAAGITCICIGIAAAGAACAIGAATGIAATAIAAGAIGAGGIGAAAAAIGTIIAITICAA 428 IGAAGI ICICTGTAAAGAACATGAATGTAATATAGATGAGGTGAAAAADGTITATTTCAA 99.8%; Score 3447; DB 19; Length 3555; \mathbb{R}_T abnormal cellular proliferation, particularly cancers. slopul Sequence 3555 BP; 1171 A; 684 C; 653 G; 1047 T; 0 other; 0 0; Mismatches Pred. No. 0; 100.0%; Conservative Similarity Mutches 3447: Dong Match Ş 4 <u>a</u> 3 2 ŝ = Š 3 ب ŝ ÷ £ 4 Ś 2 5 3 Ξ ŝ

1008 ATTATTTTGGATCATGATAAAACTCTTGAGAGTGAIICTAIAGAGAGIIIIGGAAAGAGA 1067 1269 CCGAGTAATGGAAICCATGCTTAAATCAGAAGAAGAACATTATCAAATTTTAG 1328 1509 TTTTATCAAAGCAGAAGGCAACTTGACAAGAAATGATAAAAQATTAGAAAGATTAGAAAGATATAA 1568 1569 ACAICGAATCATGGAATCCTTGGATGGCTCTCAGATTCACCTTATTTGATCTTATTAA 1628 1728 ACAAICAAAGGAGGGAGAAGGACCAAQIGAIGAGGIIGAAIGIGGGIIGIGGCTTIAATGI 1787 1788 TCCFCCCAGAATAATCACACTGCAGCAGATATGTATCTTCTCCTGTAAGATCTCCAAA 1847 1869 GTATCOCCTATCTCCGCCTAATACACTTTGTGAACGCCTTCTCTGACCACTT 1928 969 GASAACACTACTAAAAAAAAATAAACTTGALGAAGAGTCTAAATGTAATTICCTCCACACICC 1188 TCAACCTTCAGAAAATCTGATTTCCTATTTTAACAACTGCACAGTGAATCCAAAAGAAAC 1368 CCGAGTAATGGAATCCATGCTTAAATCAGAAGAAGAATATGCATTATCAAAATTTTAG 1449 CCCATGGATTCTGAATGTGCTTAATITAAAAGCCITTGATTTTACAAAGTGATGGAAAG 1548 CCCATGCATTCTGAATGTGCTTAATTTAAAAGCCTTTGATTTTTACAAAGTGATGGAAAG 849 TGAAAATCTTTCTAAACGATACGAAGAAATTTATCTTAAAAATAAAAGATCTAGATGCAAG 1068 GAGAACACCACGAAAAAGIAACCIIGAIGAAGAGGGIGAAIGIAAIICCIGCACACACICC 1029 AGTTAGGATGTTATGAAGAGTAFGCAAGAAITAATGAFGAFTTTAAATTGAGGAAGTGA 1248 TATACTGAAAAGAGGAGGATATAGGATACAICTITAAAGAGAAATTTGGTAAAGGTGT 1209 GOGANGAGOTO FOR ANATIGGAT CANAGORA ACARACIT GOAGOT CONTRATATION 1329 CAAACTTCTGAATGACAACATTITTCATATGTCTTTATTGGCGTGCGCTCTTGAGGTTGT 1629 ACAATCAAAGGACCGAGAAGAACCAACTGAACCTTGAATCTGCTTGTCCTCTTAATCT 1689 TCCTCTCCAGAATAATCACACTGCAGATATGTATCTTTTCTCCTGTAAGATCTCTAAA 1809 AGCCTTCAGACCAGGACCATGAAATCTACCTCTCTTTCACTGTTTTATAAAAAGT 909 AITATITITGGAICAIGAIAAAACICIICAGACIGAIICIAIAGACAGII11GAAACAC 1428 CAAACTICIGAAIGACAACAITIIICAIAIGICIITAIIGGGGGGGGGCTICIIGA 1389 AATGGCCACATATAGCAGAAGTACATCATCATGATTCTGGGAACAGATTTGTCTT 1848 GAAAAAAGGTTCAACTTACCCTGTAAATTCTACTGGAAATGGAGAGACACAAAGGAACT 1968 GTATGGGCTAGCCTATCTCCGGCTAAAIACACTTTGTGAAGGGGTTGTGTGTGTGAGGAGG 1149 TATACTGAAAAGAGTGAAGGATATAGGATACATCTTTAAAGAGAAJTTGCTAAAGCTGT 1749 GAAAAAAGGTTCAACTACGCGTGTAAATICTACTGCAAAIGCAGAGACACAAAGCAAAAC ac . qq q ò ó d q

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5 1	4949	POLICO AAAA JAAAA LIGU DIDIGO HILA I GALAGAA AA AAAAA GOO CAAAA JAAAAA JAAAAA JAAAAA JAAAAA JAAAAA JAAAAA JAAAAA JAAAAAA	3008 '
5	6003	CDGATAACOCAGGCTGTCTGACTACTTGCCTCTTTTGGTAGGATATAGGTGATGTT	306B

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hEST2, telomerase, catalytic submit, reverse transcriptuse, life span; retinoblastoma; p53; tumour suppressor; inhibitor; arterioselerosis; proliferation; immortal; tumour therapy; macular degeneration; activator;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               The invention concerns methods and readents for extending the life span, e.g. the number of mitotic divisions, of a cell. The method relies on
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        New method for increasing the proliferative capacity of cell lines comprises administering agents reversibly activating feromerase activity and reversibly inactivating Re/INK4 and/or p5.6 pathways useful in treating age related diseases.
3108 CTGATAACCCAGGCCIGTCIGACTTGCCTTCTTTGIA.8ATATAAGGGGGGTGGCTG 46.7
                                                              3168 CICITGITITIATIAATITATATGIAIATTITITTAATITTAAN ASSA 3227
                                             3249 ATTAGATTITALITTACLATIGGAATCTGATATACTGTGTGCCTTGTTTALAAAATTIIG 3308
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                                                                                                                                                                       3189 TGAACTCTTCTGCAAAAATGGATATTATTAGAAATTAGAAAAATTACTAATTTTACAA 324H
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                                                                                                                          3309 CITITAATTAAATAAAAGCTGGAAGCAAAGTATATAACCATATGATACTATCATACTAGA
                                                                                                                                                                                        Claim 5; Page 121 123; 123pp; English.
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                                                                                                                                                                                                                                                                                                                                                                                                                                     3528 TGTTTTTAAATGAGGATTATTGATAGT 3554
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intration of a foldoworase artivity and inhibition of one or both of go net incoming account of the problem of the problem of the problem of the division cycle. Binding of INK4 family members, e.g. the tumour suppressor pickness, cold and olds, releases the reliation of Rb division cycle. Binding of INK4 family members, e.g. the tumour suppressor pickness in division excless pickness in a cold library respectively and reversibly inactivate an Rb TW4 fathway respectively and reversibly inactivate and Rb TW4 fathway respectively and reversibly inactivate and Rb TW4 fathway respectively and reversibly inactivate and Rb TW4 fathway respectively and reversibly inactivate and Rb TW4 fathway respectively and reversibly inactivate and Rb TW4 fathway respectively and reversibly inactivate and Rb TW4 fathway respectively of Rb/TV2 fathway the energy respectively of the fathway inactivate and for reliation of the methods are used in the method and for other which bypasses Rb and/or p53. Antisense constructs of the Kb and pickness may also be used. The methods are useful for increasing the proliferative capacity of cells. The cells are stablemently of use in pharmaceutical and cosmetic preparations used to replace tumour cell three in vitro and for studies on blockemical and physiological aspects of new in the production of normal or genetically engineered.

Sequence 4839 HP; 1534 A; 902 C; 880 G; 1523 T; 0 other;

308 69 ACCTGATITTACTGCAITATGTCACAAATIAAAGAIAAFAATGAGAGTGATGTCAGAGAGAGAGC 128 129 IIGGITAACITGGGAAAAGPFFATFIGGGAFTAGGAAGTTTGGGAGGTFATATTCAAAA 188 189 GAAAAAAAAACIGTGGGGAATGTGTTTATTGCAGCAGTTGAGGTGAGATGAGATGTC 248 179 OFFICACITITACTGAGGGAGGGAAAAAATAGAAATGAGTGTGCATAAATTCTTTAACTT 538 4.29 SACACACACACAGAGGGTTCGGTATCTACTGAAATAAATTCTGCATTGGTGAAAAAAGTTTC 488 779 FICATTICAGITTAATGCTATGTGTGTGTTTGACTATTTTAAAACTCTCACCTCCCATGTT 838 609 GUCAAAGAACATATAAAACAGUGITATACAGITAATGGITGAAGGAAGAACGGA 668 45.9 GTAFGATGTAFTFGCACPCTTCACCAAATFFGGAAAGGACAFGTGAACTFFAFATFTF 428 549 IIGALIIGAGIIAAIIGCEAFGEGTGGTTGACTATTTAAAGTCTCAGGTGGCATGTF 608 Gaps 9 32AGGAPANPGGCCCGGAGGAPPTPPPPPPPPAGGCTTGAGTTTGAGAAGAAGAAGA 68 249 STICACTITIACIGAGCIACAGAAAAACAIAGAAATCAGIGICCAIAAAIICITIAACIT 3.9. ANTAAAABAAATIGALACCAGTACCAAAGTTGATAATGCTATGTCAAGACTGTTGAAGAA OF ANTAAAAAAATIGAIACCAGIACCAAAGIIGAIAATGCIAIGICAAGACIGIIGAAGAA 489 I FÖGA FOAFITIT FATTAGGTFAAAGGGGAAGTATTAGAAATGGAAGATGTTGTGGTGAT 719 TIGGAICACATITITATIAGCIAAAGGGGAAGTAITACAAATGGAAGTGTGGTGAT 0 DB 21; Length 4839; 0; Indels 100.0%; Preu. 99.8%; Score 3447; Best focal Similarity 100.0 Matrics 4447; Conservative ŝ ŝ <u>a</u> ŝ ÷; Š <u>د</u> آ. :5 :7 <u>></u> ŝ

019 NAMITITARACOTITIANSAATICIGIISGACIIGIAAACALCIAALGGACTICGGAGGT 1078 959 TGAAGTEGETATERAAGAAGAAGAATGTAATATAGATGAGGEGAAAAATGTTTATTEGAA 1018 1079 TGAAAATCTTTCTAAAGGATACGAAGAAATTTATCTTAAAAATAAAGATCTAGATGCAAG 1138 969 GAGAACACCACGAAAAAATAACCIIGAIGAAGAGGTGAAIGIAAIICCICCACACACACTCC 1528 1199 GAGAACACCACAAAAAAGTAACCTIGAIGAAGGGGGAATGTAATTCCTCCACACACTCT 1258 1029 ACTTAGGACTGTTATGAACACTATCCAACAATTAATGATGTTTTAAATTCAGGAAGIGA 1388 1089 TCAACCTICAGAAAAICIGAITICCIAIIITAACAACIGGAGAGIGAAICGAAAAAAAA 1148 1209 GGGAÇAĞGGERIĞIYĞIYGIRGAAATIYGGATÇAÇEĞATAÇAAĞIYIĞEAZIYTEĞETIYETALIA 1268 1269 CCGAGIAAIGGAAICCAIGCIIAAAICAGAAGAAGAACGAIIATCCATICAAAAITIIAG 1328 1449 CCCATGGATTCTGAATGTGCTTAATTTAAAAGCCTTTGATTTTTACAAAGTGATCGAAAG 1508 1509 TITTATCAAAGCAGAAGTIGACAAGAAAATGAIAAAACAITTAGAAGGAIGISA 1558 1799 ACATCGAATCATGGAATCCCTTGCATGGCTCTCAGATTCACCTTTATTTGATCTTATTAA 1858 1629 ACAATCAAAGGACCGAGAAGGACCAACTGATCACCTIGAATCTGCTTGTCTTTAATCT 1588 1689 TOTTO CAGAMIANICACACIGCASCAGINISIALCIIICICIGIAAGAICHOCAAA 1748 1919 TOCTCTOPAGAATAATOAAGAAGTAGAGATATATATATOTTTOTOTOTATAAGATOTOGAAA 1978 1749 GAAAAAAGGWTCAACTACGCGTGTAAATTGTAALGGAAALGGAGAGAGAGAAGGAAAGGAAAGGAAAGGAAAGGAAAGGAAAGGAAAGGAAAGGAAAGAAAGAAA 1439 GGGACAGGGTTGTGGAAATTGGATGACAGGATAGAAGTGGGAGTTGGTTTGTTA 1498 1389 AATGGCCACATATAGCAGAAGTACATCTCAGAATCTTGATTCTGGAACAGALTIGICTLL 1448 1739 TITTATCAAAGAAGAGAAATIGACAAGAAAAIGAIAAAAAAITIAGAAGAGAGA 1748 1569 ACATICGAATICATIGGAATICCCITTGCTTGCTCTCAGATTCACCTTTTATTTTGATCTTATTAA 1628 849 IGAAAA1CIIICIAAACGATACGAAGAATTTATCTTAAAAATAAAGATCTAGAAGAGAGG 909 ATTAITITIGGAICATGAIAAAACICIICAGACIGAIICIAIAGACAGIIIIGAAACACA 968 729 IGAAGTICICIGIAAAGAACAIGAATGIAATATAGAGGGGGAAAAATGITIATITGAA 788 769 AAATTTATAOOTTIIAISAATTOIOTIGGAGTIGIAACATOTAATGGACTIOOAGAGGT 848 899 HITAGGICAGAATAGGATGGATAGGAAAAGAAGAACIAGAAAATGATACAAGAATIAT 958 GEG GOGAÇÇI GAGAAÇAÇAÇI ÇONÇERI NƏCARANGAN ÇINGANAMI ÇETAÇANGANI INI 1149 TATACTGAAAAGGGTGAAGGATATAGGAIACATCTTTAAAGAGAAATTTGCTAAAGCTGT 1619 NATGGCCACATATAGCAGAAGTACATCTCAGAAICIIGAIICTGGAANAGAIIIGICIII 1679 CCCATGGATTCTGAATGTGCTTAAAAAGCCTTTGATTTTTAGAAAGTGALGGAAAG 1499 COGAGTAATGGATGGTTAAATGAGAAGAAGAAGATTATCCALICAAAALLILAG 1329 CAAACITCIGAAIGACAATTIIICAIATGICIIIAIIGGCGIGCGCTCIIGAGGITGI ŷλ ċ Ś ç ζ ô qq ò D) qu d Öλ qq q ŏ qq 급 à ें 合 d ò a à